HEMATOLOGICAL ATLAS

WITH A

DESCRIPTION OF THE TECHNIC

OF

BLOOD EXAMINATION

BY

Priv. Doz. Dr. Karl Schleip

Scientific Assistant in the Medical Clinic University of Freiburg i/B.

ENGLISH ADAPTATION OF TEXT

BY

Frederic E. Sondern, M.D.

Professor of Clinical Pathology New York Post Graduate Medical School and Hospital,
Director of Clinical Laboratory New York Lying-In Hospital.

With 71 Colored Illustrations

NEW YORK
REBMAN COMPANY
1123 BROADWAY

Printed in America

Dedicated to

GEHEIMRAT PROFESSOR DR. CHR. BÄUMLER

PREFACE TO THE ENGLISH EDITION

The paucity of good pictures illustrating the changes in the microscopic appearance of the blood which have become apparent by the use of panoptic staining methods is evident to the teacher of Clinical Hematology. To this fact noted by the author, and to the opportunities offered him by the hematological material available at the Medical Clinic of the University of Freiburg, this Atlas owes its origin. An accurate picture of characteristic changes is often better than a detailed description or an imperfect specimen.

The object of the Atlas is not only to assist in teaching the subject but also to serve as a guide for the private study of the clinician; and the brief diagnostic points and explanatory comments may be of value in this connection. In the nomenclature of the blood cells the universally used terms have been selected, and those based on theories not yet firmly established have been avoided.

A sufficiently detailed technic of the clinical methods used in blood examination has been included with the hope of enhancing the usefulness of the book, and the complicated procedures demanding extensive apparatus and not suited to the use of the clinical worker have been omitted. The original illustrations represent specimens stained with the *Leishman* modification of the *Romanowsky* method, and uniform magnifications of 330 and 750 only have been used.

Few slight changes have been made in the English adaptation of the text where these seemed indicated by different customs and racial characteristics, but classifications, nomenclature, etc., are strict translations of the original.

FREDERIC E. SONDERN.

New York City.

TABLE OF CONTENTS

PAGE

EXAMINATION OF THE BLOOD BY CLINICAL METHODS 1–12

Obtaining the Blood and Preparation of Dried Films 3
Estimation of the Amount of Hemoglobin . . 4
Counting the Blood Corpuscles 5
Differential Count of Leucocytes 9
Examination of the Fresh Blood 10
Staining the Dried Films 11
Estimation of the Specific Gravity 12

DEVELOPMENT OF WHITE AND RED BLOOD CORPUSCLES 15–21

Plate I

NORMAL BLOOD 23–31

Plates II–III

THE WHITE CORPUSCLES OF THE HUMAN BLOOD . 33–55

Plates IV–VII

THE VARIETIES OF LEUCOCYTOSIS . . . 57–85

Plates VIII–XIII

Neutrophilic Leucocytosis 59
Eosinophilic Leucocytosis 67
Leucocytosis in Children 75
Lymphocytosis 81

THE RED CORPUSCLES OF THE HUMAN BLOOD AND BLOOD PLATELETS 87–93

Plate XIV

THE ANEMIAS 95–137

Plates XV–XXII

Polychromatophilia 97
Basophilic Granulation 103

PAGE

Secondary Anemias 109–123

Primary Anemias 125–137

Chlorosis 131

Pernicious Anemia 135

Leukemias 139–215

Plates XXIII–XXXVII

Chronic Lymphatic Leukemia 153

Myelogenous Leukemia 173

Acute Leukemia 207

Blood Changes Associated with Tumors of the Bone Marrow 217–231

Plates XXXVIII–XL

Carcinoma of the Bone Marrow 219

Sarcoma of the Bone Marrow 225

Leukosarcomatosis 229

Blood Parasites 233–257

Plates XLI–XLV

Tertian Malaria 239

Quartan Malaria 249

Estivo-autumnal Malaria 249

Trypanosomiasis 253

TECHNIC OF CLINICAL METHODS

FOR

EXAMINATION OF THE BLOOD

Obtaining the Blood and Preparing the Dried Films

The blood is usually obtained from the lobe of the ear or the tip of the finger by a rapid puncture with one of the various blood lancets or a straight *Hagedorn* needle of medium size. Experience develops good technic and if the procedure is rapid there is practically no pain or subsequent discomfort. Previous cleansing of the skin is desirable, for by thus softening it the puncture is more easily made. The blood should flow slowly of its own accord and without pressure on the immediately surrounding tissues. The first drop of blood and any moisture of the skin should be wiped away and the following small drop taken up on the surface of a cover-glass very close to its edge. A slide, which has been carefully cleaned, is held by the left-hand end and the edge of the cover-glass placed in contact with it at the other end, and inclined to the right until the blood drop also touches the slide and spreads the entire width of the cover-glass.

Held in this position the cover is now rapidly pushed over the surface of the slide toward the left hand, the drop being drawn along behind it. Any injury to or distortion of the corpuscles is avoided by this method, as no pressure is used, and while the resulting spread is rather thick where begun, it is quite thin and uniform toward the middle and left end of the specimen.

Several precautions should be observed. The cover-glass should not come into contact with the skin while it is being charged with blood, and the smaller the amount used, the better the resulting film.

The cover-glass used for spreading must have an absolutely smooth edge, otherwise the leucocytes may be distributed unevenly, thus jeopardizing the accuracy of the differential count. The whole procedure should be accomplished as quickly as possible so that comparatively little time elapses between the appearance of the drop of blood and the drying of the prepared films.

Estimation of the Amount of Hemoglobin

In the application of clinical methods in blood examination, several procedures and appliances for determining the amount of hemoglobin must be considered. There are numerous good methods, but none as yet without some disadvantage. In most of the clinical methods employed, the diluted blood is compared with some artificially colored substance. In the *Fleischl-Miescher* hemometer this substance consists of a wedge-shaped piece of stained glass while in the *Gower's* hemoglobinometer a glycerin jelly stained with piero-carmin is used. Both of these methods are trustworthy and universally used, but the new *Sahli* hemometer deserves special mention.

The Sahli Hemometer

The inference is reasonable that the best colorimetric determination can be made by comparing the solution to be tested with one of known strength containing the identical pigment. While a solution of hemoglobin would be the ideal standard, this is not feasible on account of its rapid deterioration. Consequently, *Sahli* employs a stable hemoglobin derivative as a standard, and converts the blood to be examined into the same derivative before the determination is made. The principle is as follows: One part of blood is mixed with ten parts of decinormal hydrochloric acid in a graduated tube, with the result that an acid hematin is obtained, quite constant in

color and composition. This dark brown fluid dilutes to a clear yellow with water and is well adapted to colorimetric estimation. The standard solution is sealed in a comparison tube of exactly the same caliber and corresponds to a 1 per cent. solution of normal blood.

To apply the test, the graduated tube is filled with decinormal hydrochloric acid to the 10 per cent. point, to which 20 c.mm. of blood obtained with the capillary pipette is added, and the whole carefully shaken. As soon as the mixture assumes a clear dark brown color, water is added drop by drop until the tint corresponds to that of the standard tube. The percentage of hemoglobin is read from the point of the scale corresponding to the height of the solution.

Counting the Blood Corpuscles

It is very essential that the blood used for this purpose be taken as quickly after the puncture as possible with accurate technic, in order to avoid sources of considerable error. The *Thoma-Zeiss* counting chamber can be recommended for the separate estimation of red cells and leucocytes, but for greater convenience and accuracy in the leucocyte count or when leucocytes and red cells are to be counted in the same preparation, the chambers ruled according to *Zappert* or *Türk* are preferable.

Diluting Fluids

In order to count the red corpuscles it is necessary to dilute the blood with a fluid which will prevent coagulation and cause no change in the cellular elements. One of the following may be used:

Hayem's Solution:

	Gram
Bichloride of Mercury	0.5
Sulphate of Sodium	5.0
Chloride of Sodium	1.0
Distilled Water	200.0

Toisson's Solution:

	Gram
Methyl Violet 5 B	0.025
Chloride of Sodium	1.0
Sulphate of Sodium	8.0
Glycerin	30.0
Distilled Water	160.0

For the purpose of counting the leucocytes a diluting fluid is required which lakes the red corpuscles and not only preserves the white cells but also makes their nuclei more distinct. This is accomplished by the use of 0.3 to 0.6 per cent. solution of glacial acetic acid to which a few drops of concentrated aqueous solution of gentian violet may be added to stain the nuclei.

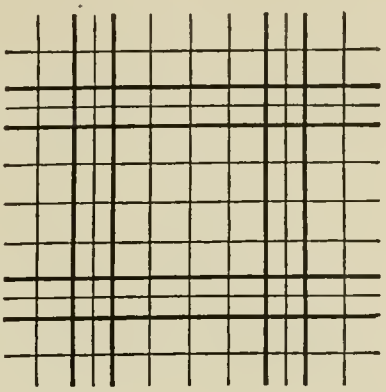
Counting the Red Corpuscles

The *Thoma-Zeiss* hemocytometer consists of the following:

1. *The Mixing Pipette* is a graduated thick-walled capillary tube pointed at one end and dilated into a bulb at the other, with a short tube at the opposite pole of the bulb to which the rubber aspirating tube is attached. The bulb contains a small glass ball to facilitate the mixing. The capillary tube bears the graduations 0.5 and 1.0 and the upper end of the bulb is marked 101, indicating that the capacity of the bulb is 100 times that of the capillary tube.

2. *The Counting Chamber* consists of a heavy glass slide on which a square glass plate, with a circular opening 1 cm. in diameter, is cemented. A circular glass disk 8 mm. in diameter is cemented in the center of this opening in such a way that a ditch separates the two, the slide forming its floor. The surface of the central disk is exactly 0.1 mm. lower than the level of the outer glass plate and forms the floor of the counting chamber. Its center is ruled in such a way that 400 small squares are formed each having an area of $\frac{1}{400}$ sq. mm. An extra line is ruled through each fifth row of squares, as shown in the accompany-

ing illustration, to facilitate the counting. The upper limit of the chamber is formed by a superimposed absolutely plane cover-glass.



The red cell count is made as follows:

After the puncture, made in the usual way, a rather large drop of blood is allowed to collect, and this is rapidly drawn into the pipette to the mark 1.0. After wiping the point, it is plunged into a bottle containing the diluting fluid. While this is being drawn into the bulb the pipette should be twirled between the fingers to mix the blood and diluting fluid. When the mark 101 is reached, aspiration is stopped, the rubber tube removed, and with the thumb on the point and the middle finger closing the other end, the whole gently shaken. Some experience is necessary before perfect technic is acquired. As the fluid remaining in the capillary tube does not enter into the mixture, the bulb now contains 1 part blood and 99 parts diluting fluid. If the blood has been drawn to the mark 0.5 the dilution is 1 in 200, instead of 1 in 100 as above.

The rubber tube is again attached, a few drops blown out, the point wiped dry, and the next small drop placed in the center of the scrupulously clean counting chamber, over which the polished cover-glass is placed with some pressure. If the contact is perfect, as it must be if accurate results are desired, the *Newton's* rings are visible. The drop used must not be too large or some of it will fill the ditch and run between the cover and the outer glass disk. In this case it is necessary to repeat the procedure with a smaller drop.

The slide is now left undisturbed for about five

minutes to allow the corpuscles to settle on the bottom of the chamber. The counting of the corpuscles is best done with a magnification of about 300, which presents a good picture of the network of squares. The area of each small square is $\frac{1}{400}$ sq. mm., and the distance between the floor and the lower surface of the cover is $\frac{1}{10}$ mm., consequently each square represents $\frac{1}{4000}$ cu. mm. The cells in a large number of these squares are now counted, including those which touch or overlap the upper and left-hand boundary lines, but not those which touch or overlap the lower and right-hand boundary lines. With proper technic the corpuscles are uniformly distributed and counting those in 100 small squares is usually sufficient. If a dilution of 1:100 has been used, the calculation will be as follows: Supposing 1,450 corpuscles were counted in 100 small squares, each square will average $\frac{1450}{100}$ corpuscles. As each square represents a height of $\frac{1}{10}$ mm. and a surface of $\frac{1}{400}$ sq. mm., each cubic mm. contains $10 \times 400 = 4{,}000$ times as many cells. A dilution of 1:100 having been used the blood contains 100 times as many cells as the dilution. Therefore the formula for the calculation will be,

$$\frac{1{,}450 \times 4{,}000 \times 100}{100} = 1{,}450 \times 4{,}000 = 5{,}800{,}000$$

red corpuscles in 1 cu. mm. of blood.

The careful cleaning of the pipette is important, and this is accomplished by putting the rubber tube on the capillary tube end of the pipette and drawing water through it. This is followed by alcohol and then by ether, the latter being allowed to run out first one end and then the other by itself. Air is then sucked through by mouth or aspirator until the interior is dry. The counting chamber is rinsed in water only.

Counting the Leucocytes

For the enumeration of the leucocytes, large bore pipettes are usually employed, with a resulting dilu-

tion of 1:10 or 1:20, the bulb holding but 10 times as much as the capillary tube. After the dilution with the acetic acid solution has been made, the procedure is the same as in counting red corpuscles.

For reasons mentioned, a chamber with *Zappert* ruling should preferably be used for leucocytes, as it admits of counting 2,000 small squares in one specimen. Supposing the dilution was 1:10, and 2,000 squares were counted, the calculation would be

$$\frac{X \times 4{,}000 \times 10}{2{,}000} = X \times 20.$$

Extreme care and accuracy are absolutely essential in every blood cell count, if the result is to be correct. Beginners cannot possibly avoid all sources of error, and practice is undoubtedly necessary before a proper and uniform technic can be acquired.

The Differential Count of Leucocytes

Owing to the development in the knowledge of blood changes in disease, a proper estimation of the condition of the blood usually demands information concerning the relative percentage, or the absolute number, of the different varieties of leucocytes present, in addition to the total leucocyte count. Fluctuations in the quantitative relation of the various forms are not uncommon and may present a differential count suggestive or pathognomonic of a given disease. In other cases, valuable prognostic data may be derived from the differential count.

Evenly spread and stained blood films are employed for the count, and the use of a mechanical stage is desirable. The easiest method of tally is to have another person note the cells as called, but in the absence of such help the number of neutrophiles may be kept in mind and the other varieties noted on paper. With a little practice every one usually devises a convenient scheme. A minimum of 300, but preferably 500, cells should be counted in order to

secure approximately reliable results. The relative or percentage value of each variety is then figured, and the absolute count should also be determined, by applying the percentages to the total leucocyte count made by means of the counting chamber.

While making the differential count, the character of the red blood cells, the approximate number of blood platelets, and the presence or absence of nucleated red cells or plasmodia of malaria should also be noted.

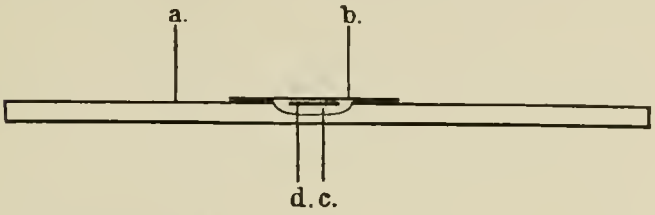
Examination of Fresh Blood

The examination of fresh blood in its moist unstained state is frequently conducted in an improper manner. When a drop of blood is examined between slide and cover-glass, evaporation and mechanical injury are apt to occur, and the degree of poikilocytosis, for example, cannot be properly estimated. Under these conditions the use of an oil-immersion objective is also difficult, as the cover-glass may float on the layer of blood.

The following procedure is recommended: A ring of cedar oil is applied around the edge of the concave depression in a hanging drop slide. A perfectly clean square cover-glass is prepared and a likewise clean small piece of cover-glass about 4 mm. in diameter is placed on the center of it. The large bore *Thoma-Zeiss* pipette is then filled with fresh blood and diluted in proportion of 1:10 with physiological salt solution. After mixing and blowing out a few drops, a little of the diluted blood is allowed to run between the two cover-glasses, as prepared, and the inverted concave slide placed in such a position that the oil ring is in perfect contact with the larger cover-glass. The specimen is then turned right side up and has the appearance as illustrated.

The completed specimen of diluted blood is thus prepared in a way which certainly prevents evaporation and mechanical injury. The capillary layer is

preferable to the hanging drop, and the dilution is employed, as it permits a more careful study of the shape of individual corpuscles than is possible when undiluted blood is examined. The specimens may be examined with a low or high power, and if kept



a. Slide with concave center.
b. Large cover-glass.
c. Chamber made air tight by the layer of oil between *a*. and *b*.
d. Small piece of cover-glass, held to the under surface of *b*. by the intervening capillary layer of blood.

warm will show all the characteristics even after the lapse of hours. The excellent results obtained by means of this method are well shown in Table II, Figure 3. Staining fluids may be added to the diluting solution for the easier recognition of leucocytes, five drops of an aqueous solution of gentian violet to each 10 c.c. of salt solution being recommended.

Staining the Dried Films

The *Romanowsky* method, or one of its numerous modifications, is in almost universal use at present for staining dried blood spreads. For some years the author has used the *Leishman** modification almost exclusively. This is an eosinate of methylene blue dissolved in methyl alcohol, which fixes and stains the specimens simultaneously. The *Leishman* is a panoptic stain, and preferable on account of the simplicity of the procedure. It is used as follows: The air-dried blood film, without previous fixation, is covered with about ten drops of staining fluid. After about thirty seconds, double this amount of

**W. B. Leishman.* A Simple and Rapid Method of producing *Romanowsky* Staining in Malaria and other Blood Films. British Med. Journ., Sept. 21, 1901.

distilled water is added to and mixed with the stain. Five minutes later the mixture is washed off with water, and the slide dried between lintless blotters. If the specimen is overstained, the erythrocytes have a deep red or greenish tint. This can be remedied by allowing a few drops of distilled water to remain on the slide for one or two minutes, after which it is washed and dried as before. The entire procedure of spreading the blood, drying, staining and placing the specimen under the microscope should not consume more than seven or eight minutes. Only one reagent and a little distilled water are needed for the staining. The results of the method are shown on the following pages, and particular attention is called to Plates IV, V and XV.

The stained specimen can now be studied with a low power or with an immersion lens, a permanent mounting in balsam being unnecessary. If balsam is used, it is well to remember that an acid balsam decolorizes the specimen after a time. The cedar oil used on unmounted specimens can be removed with xylol without injury to the blood film.

Estimation of the Specific Gravity

A knowledge of the concentration of the blood is of considerable importance in a number of diseases. The experienced observer will immediately note decided changes in this respect by the appearance of the blood, which observation is sufficiently accurate to determine the degree of dilution best suited to the general blood examination about to be made.

The *Schmalz* method of determining the specific gravity by means of a capillary pycnometer is useful and accurate, but requires experience. A glass tube about 10 cm. long, constricted at both ends and holding 0.2 c.c. of fluid, is weighed empty on an accurate balance sensitive to 0.1 mg. It is then filled with distilled water and again weighed. The difference

represents the weight of the water held by the tube. After thorough drying the tube is filled with blood and the outer surface carefully cleaned. The net weight of the blood divided by the weight of the water will indicate the specific gravity of the former. The normal specific gravity of the blood is variously stated, but averages 1052 to 1058 in men and 1048 to 1055 in women.

DEVELOPMENT

OF

WHITE AND RED BLOOD CORPUSCLES

PLATE I FIGURE 1

PLATE I

Figure 1.—The Development of White and Red Blood Corpuscles

The normal and pathological cells of the human blood all probably originate in the bone marrow, with the exception of the lymphocytes. Of these a small number are derived from the bone marrow, but by far the larger number come from the lymph glands.

A previous study of the manner of development of the different cells according to the generally accepted theory, will lead to a better understanding of the clinically important changes in the blood, the significance of individual cells and the relations they bear to one another.

All human blood cells can easily be traced to one parent form (1). An unbroken series of cells representing successive stages of development are found between this parent form and the normal cells of the blood. The cells closest to the parent form show different characteristics at an early period by assuming either a basophilic (2) or a neutrophilic (3) protoplasm. Subsequently, these cells develop into other forms (4 and 5), constituting, on the one hand, a transition into the mature neutrophilic granular cells of the bone marrow (6), the so-called neutrophilic myelocytes, and, on the other hand, pass, by further intermediate stages, into lymphocytes (13) and transitional forms (15). The term "transitional form" is derived from the older interpretation of this cell as a preliminary stage of the polymorphonuclear neutrophile, or as an intermediate stage between that cell and the neutrophilic myelocyte. This view is scarcely

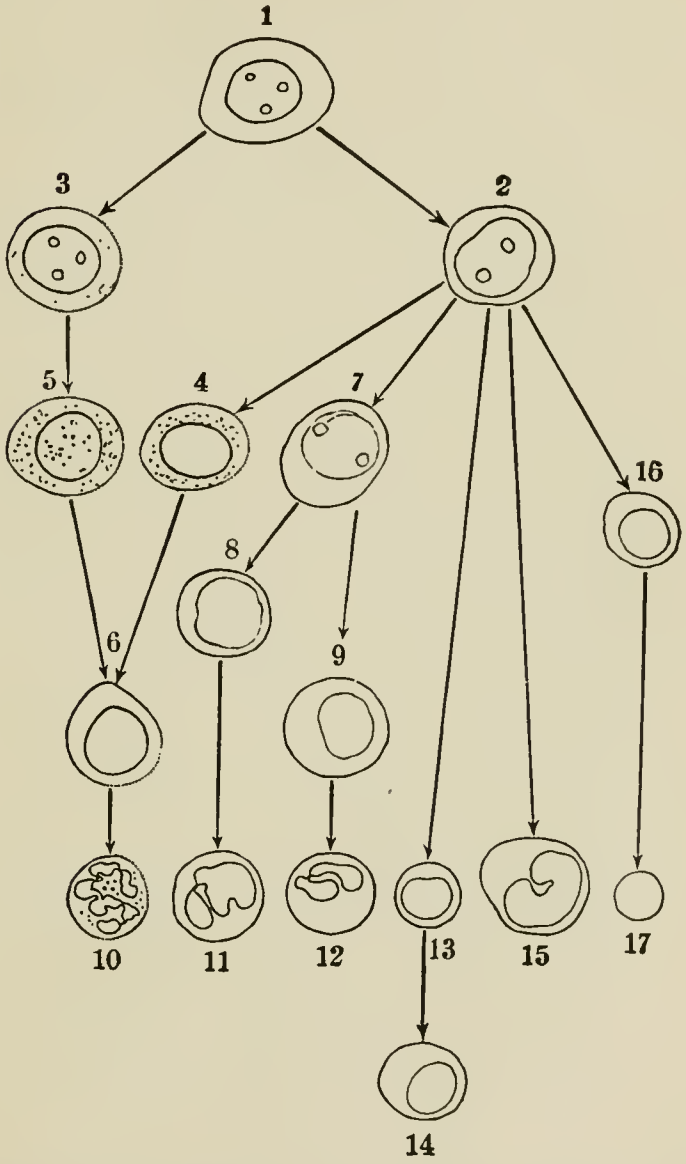
justified at the present state of our knowledge and it is probable that the transitional form also represents a terminal cellular type incapable of further development.

The large cell with homogeneous basophilic protoplasm (2) also gives rise, by way of intermediate stages, to the basophilic myelocyte (8), which in turn is transformed into the basophile (11). The eosinophile (12) may be derived, by way of the eosinophilic myelocyte (9), from the preliminary stages of the basophilic myelocyte. A close relationship probably exists between the basophilic and the eosinophilic myelocyte, notwithstanding their dissimilar staining qualities, as intermediate stages between these two cells are not infrequently encountered in leukemic blood. Basophiles are invariably found increased in cases of relative eosinophilia, and the association of these mature cells is a common clinical phenomenon.

The neutrophilic leucocyte (10) is derived from the neutrophilic myelocyte (6) in the same way as the normal eosinophile and basophile (12 and 11) develop from the corresponding eosinophilic myelocyte (9) and the basophilic myelocyte (8). The rare irritation form of *Türk* (14) is at present interpreted as a lymphocyte, the further development of which is due to a pathological stimulus, and not as a preliminary stage of the mature lymphocyte (13), as formerly believed.

The erythrocytes can also be traced, by direct transition, to the parent cell; the large mononuclear cell with homogeneous basophilic protoplasm (2) being a forerunner of the megaloblast (16). The megaloblast in its early stage may have a voluminous basophilic cell body and a relatively large nucleus and, occurring in the peripheral circulation, is often distinguished with difficulty from the *Türk* irritation form (see Fig. 41). As the result of the further development of the megaloblast, the normoblast is formed, and subsequently the erythrocyte (17).

Plate I represents a genealogical scheme of development, including the chief types only. In the designation of cells the suggestion of *Grawitz* is recommended,

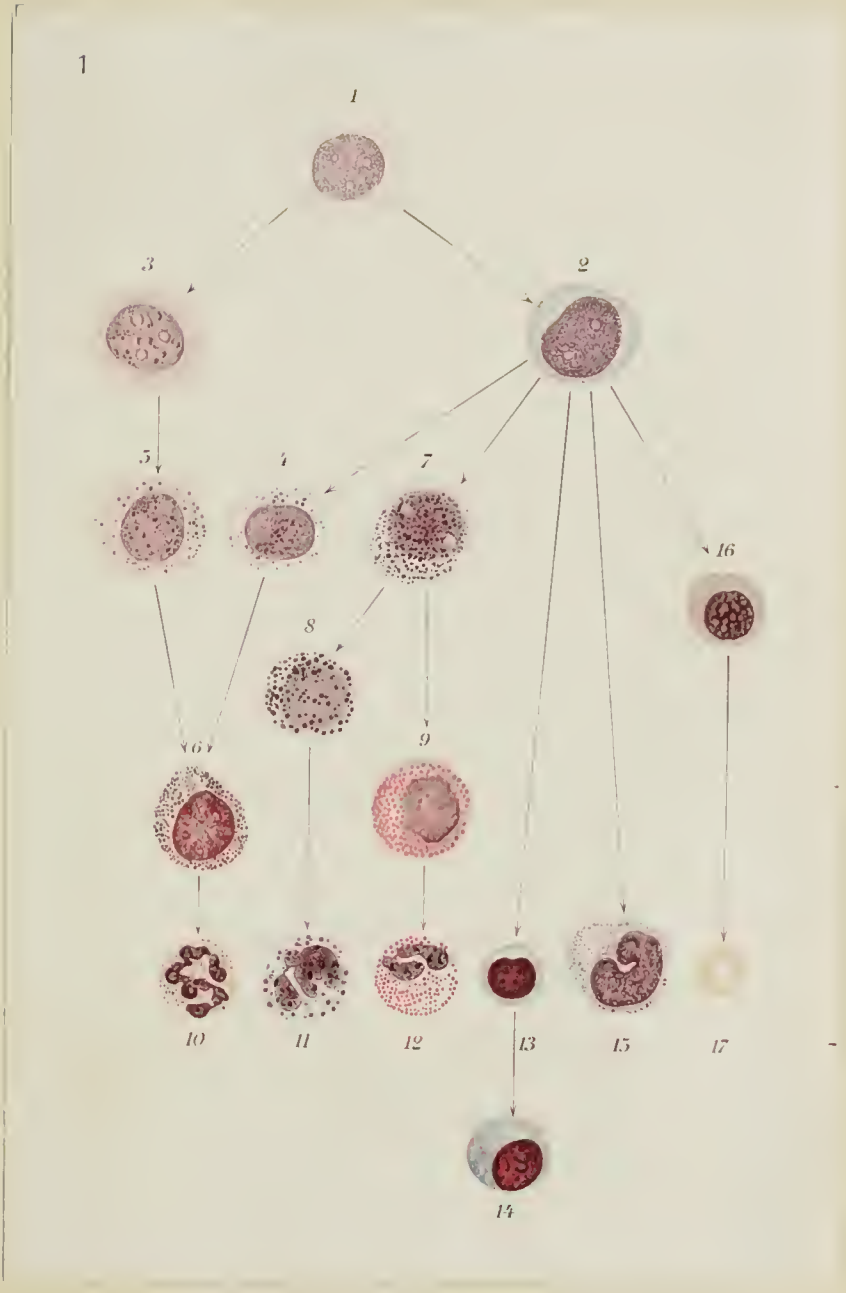


that for the present the terms having definite significance, such as "myelocyte," be adhered to, with the additional characteristic attached, for example: neu-

trophilic myelocyte, eosinophilic myelocyte, etc., rather than the arbitrary nomenclature suggested by different authors.

In the development of all blood corpuscles, the following chief forms must be considered:

1. Large mononuclear cell with pale homogeneous cell body = parent cell.
2. Large mononuclear basophilic cell.
3. Large mononuclear neutrophilic cell.
4. Mononuclear basophilic cell in which there are few neutrophilic granules.
5. Mononuclear neutrophilic cell in which there are few neutrophilic granules.
6. Mononuclear cell with dense neutrophilic granulation = neutrophilic myelocyte.
7. Mononuclear basophilic cell with beginning basophilic granulation.
8. Mononuclear cell with basophilic granulation = basophilic myelocyte.
9. Mononuclear cell with eosinophilic granulation = eosinophilic myelocyte.
10. Neutrophile.
11. Basophile.
12. Eosinophile.
13. Lymphocyte.
14. *Türk* irritation form.
15. Transitional form.
16. Erythroblast.
17. Erythrocyte.


1
1
3
2
5
4
7
16
8
6
9
10
11
12
13
15
17
14

NORMAL BLOOD

PLATES II AND III FIGURES 2-5

PLATE II

Figures 2 and 3.—Normal Blood

The blood of healthy individuals presents certain physiologieal variations within comparatively narrow limits. The average composition is approximately as follows:

Children ½ to 15 years: Hemoglobin, 70 to 80 per cent.; red cells, 4,900,000; leucocytes, 9,000 in 1 c. mm.

Men: Hemoglobin, 90 to 100 per cent.; red cells, 5,100,000; leucocytes, 7,500 in 1 c. mm.

Women: Hemoglobin, 85 to 95 per cent.; red cells, 4,500,000 to 5,000,000; leucocytes, 7,500 in 1 c. mm.

Healthy Man, 32 years old: Hemoglobin, 120 per cent.; red cells. 5,600,000; leucocytes, 7,800.

Figure 2.—Fresh Double Cover-Glass Specimen Unstained. Magnification 330

The pale yellow color of the erythrocytes is the characteristic normal hemoglobin tint. The cells are uniform in size, some appearing cup shaped on account of their position. The detailed structure is more apparent when a higher power is used.

Figure 3.—The Same Specimen. Magnification 750

Normal red blood corpuscles appear cup shaped with thickened walls. This appearance is only noted as long as injurious influences are excluded, such as evaporation, drying from any cause, hypertonia, isotonia, cold or heat, which cannot always be prevented, even by experienced workers. This cup

shape is best noted in the corpuscles lying by themselves; the convexity is apparent, and on the opposite side the concavity of the cup can be seen, its rounded margin merging into the outer wall of the blood cell.

The lateral aspect of the red corpuscle is well curved and sausage shaped, on the concave side of which there is a light transparent wall with convex margin. If the corpuscle lies so that the open end of the cup can be looked into, the appearance is that of a circle with a sharply defined, lighter colored center. This light center corresponds to the transparent crest at the floor of the cup, and the darker colored outer ring to the relatively much thicker wall of the cup.

Seen from above the corpuscle appears globular, and the cup-shaped form can only be noted on focusing a lower level. Most of the red corpuscles in the double cover-glass specimen present this appearance.

Deviations from this fundamental form are noted, but these have as yet assumed no pathological significance. The cup shape may be more or less pronounced and the opening may vary in width.

The erythrocyte is frequently seen in the form of a biconcave disk, both concavities occupied by a convex transparent membrane. This appearance is explained by the crest of the bell having become indented by contact with another corpuscle. These indentations are rarely seen in the lateral wall of the corpuscle. When the red corpuscles are close together the so-called rouleaux formation occurs as the result of crowding, the concave portion of one corpuscle slipping over the convex portion of the adjacent one. In this condition the actual form of the corpuscles cannot be made out. (See Figs. 16, 35, 37, 38, 42, 43, 46 and 51.) (*Weidenreich.*)

Three leucocytes are also seen in the field; the smallest, with a round nucleus surrounded by a narrow rim of protoplasm, is a lymphocyte. The larger

cell on the left with polymorphonuclear configuration and dense finely granular protoplasm is a polymorphonuclear leucocyte. The cell above presents a striking appearance, the nucleus consisting of several portions connected by thin nuclear strands. The protoplasm is filled with coarse, round, strongly refractive granules, some lying apparently beyond the cell but actually within protoplasmic processes of the cell, which is in slight ameboid motion. This cell is an eosinophile which is identified in the fresh specimen by its highly refractive coarse granulation.


2

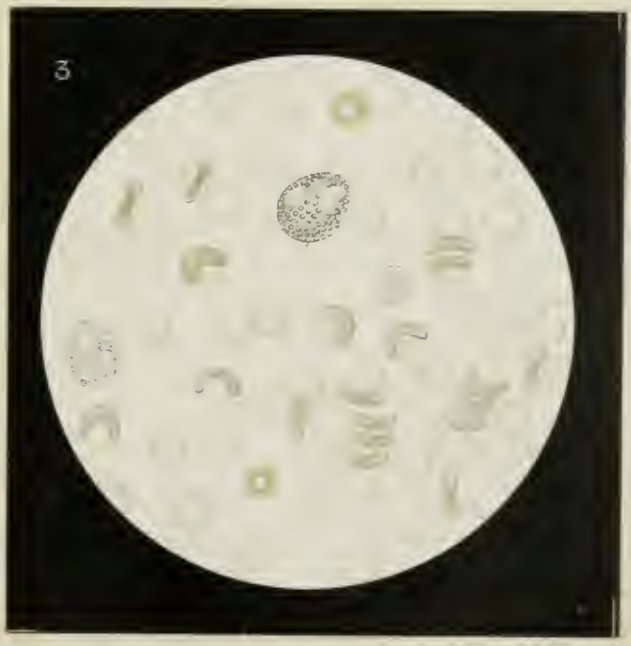

3

PLATE III

Figures 4 and 5.—Normal Blood

The same case.

Figure 4.—Stained Specimen. Magnification 330

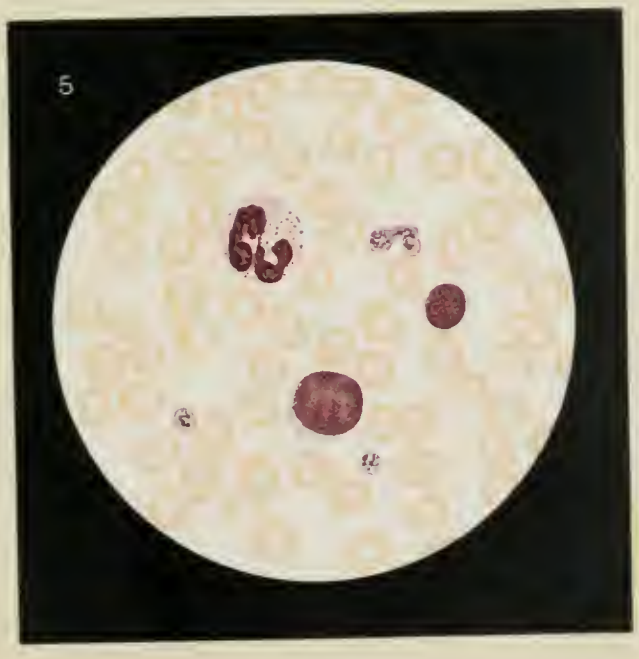
All the erythrocytes are uniform in size and, on account of being spread, are seen as flat circular yellowish-red disks, the cup shape not being apparent. While some seem uniformly pigmented, the majority have a lighter colored central zone and a darker periphery, which is due to the original cup shape of the corpuscle. The details are more apparent with the use of a higher power.

The same case.

Figure 5.—Stained Specimen. Magnification 750

The appearance of the erythrocytes is more distinct in this specimen. The depressed center, being a thin wall, is faintly stained, while the thicker edge has a deeper tone. A neutrophilic leucocyte and two lymphocytes of different size are also seen in the field.


4


5

THE WHITE CORPUSCLES

OF

THE HUMAN BLOOD

PLATES IV-VII FIGURES 6-15

PLATES IV-VII

Figures 6-15.—Leucocytes of the Human Blood

Not Including Cells of the Bone-Marrow

The number of leucocytes in 1 c. mm. of blood in an adult is approximately 7,500. These consist of a variety of different forms, which, under normal circumstances, are present in a definite numerical ratio to one another. This enumeration is known as the "Differential Count of Leucocytes," and the following are the normal varieties and figures:

Polymorphonuclear Neutrophiles	65 to 70 per cent.	or 4,900 to 5,300	in 1 c.mm.
Lymphocytes	20 to 25 per cent.	or 1,500 to 2,000	in 1 c.mm.
Transitional Forms	3 to 5 per cent.	or 230 to 380	in 1 c.mm.
Eosinophiles	2 to 4 per cent.	or 150 to 300	in 1 c.mm.
Basophiles	½ per cent.	or	40 in 1 c.mm.

Türk's Irritation Forms rarely occur.

In children under 5 years of age, the lymphocyte is the predominating cell, and the polymorphonuclear neutrophiles usually amount to less than 50 per cent.

PLATE IV

Figure 6.—Neutrophilic Leucocytes
Figure 7.—Lymphocytes
Figure 8.—Transitional Forms

Figure 6.—Polymorphonuclear Neutrophiles. Magnification 750

These cells are usually about twice the size of an erythrocyte, rarely larger. The nucleus is characterized by its polymorphous configuration, some of the portions often being connected by thin nuclear strands. Apparently separate nuclear segments are occasionally seen, but these have "underground" connection, as the cells are never polynuclear. The protoplasm is neutrophilic and shows close fine granulations which are especially apparent in cases of leucocytosis, but are occasionally so slight that they cannot be brought out even in overstained specimens. The neutrophilic quality of the protoplasm also varies, and these differences are probably due to different ages and functions of the cells, rather than to any fault in staining.

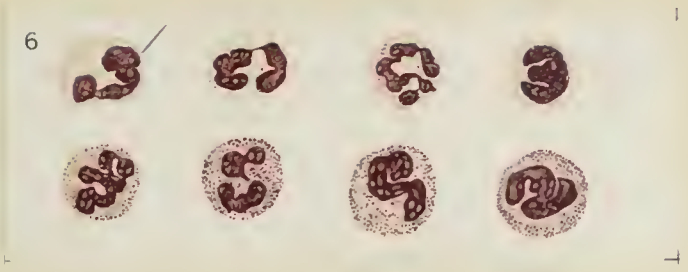
Figure 7.—Lymphocytes. Magnification 750

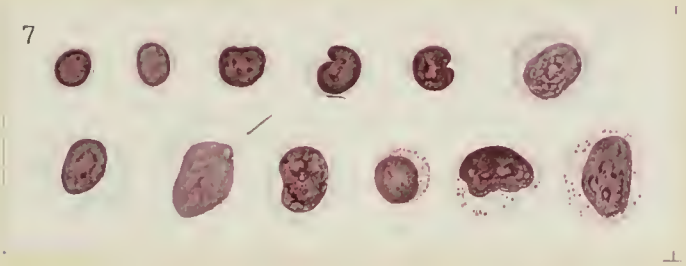
The cells are extremely varied in size and some show a narrow, others a broad ring of protoplasm. The majority are small, little larger than an erythrocyte, but very large forms, four or five times the size of the small ones are frequently seen in children, and occasionally in adults. The nucleus is usually round and sometimes indented, and in the larger forms it is oval or polygonal. It stains deeply in the small cells and rather faintly in the larger ones and two or more nucleoli may become visible. The protoplasm is slightly basophilic,—more so in the small cells than in the large ones,—and occasionally

the outer zone stains darker than that close to the nucleus. The large lymphocytes may present angular or irregular outlines. A smaller or larger number of all lymphocytes show acidophilic granulation, which appears as fine particles or angular granules. This is noted in every specimen and has no pathological significance as yet.

Figure 8.—Transitional Forms. Magnification 750

These cells are invariably larger than the polymorphonuclear neutrophiles and frequently irregularly round in outline. (The irregular outline as in the case of the large lymphocytes is probably referable to adjacent erythrocytes, or those in close proximity.) Compared with the other lymphocytes, the nucleus is always paler and poorer in chromatin. It is usually horseshoe shaped or multilobular, rarely round and indented. The protoplasm is slightly basophilic and contains more or less marked neutrophilic granulation most apparent in the nuclear indentations. With these characteristics in mind, the cells are easily differentiated from the polymorphonuclear neutrophiles.


6


7

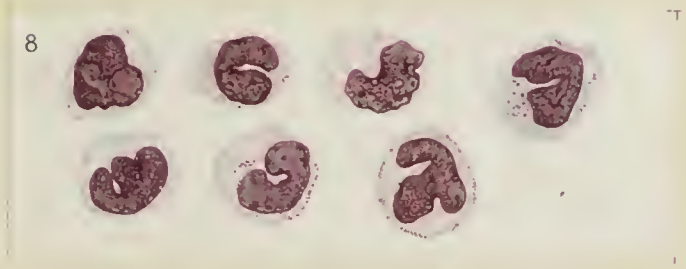

8

PLATE V

Figure 9.—Eosinophiles
Figure 10.—Basophiles
Figure 11.—Türk's Irritation Forms

Figure 9.—Eosinophiles. Magnification 750

These are very striking and easily identified round cells of the same size as polymorphonuclear neutrophiles, rarely larger or smaller. They frequently have two or three oblong or oval nuclear portions connected by thin nuclear strands, which are occasionally unequal in size.

The protoplasm is faintly basophilic and shows a bright-red coarse granulation. The granules are round, varying in number, and may be arranged in groups. Some cells are so densely filled with granules that they can scarcely be distinguished.

In one case of trichinosis, the author found a cell containing an equal number of eosinophilic and basophilic granules (see Fig. 9).

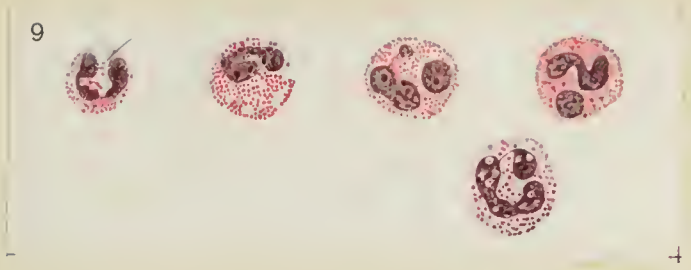
Figure 10.—Basophiles. Magnification 750

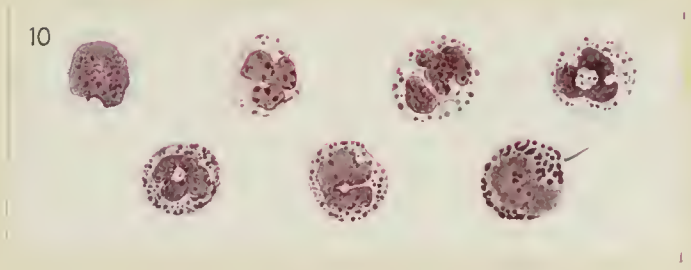
These cells vary in appearance and are about the size of an eosinophile. They occur less frequently, and are not as easily recognized. The nucleus occupies about two-thirds of the cell, usually presenting the outline of a clover-leaf or rosette, rarely round or indented, with no defined margin. The protoplasm shows a fine basophilic or eosinophilic network. Round coarse granules of varied size are seen at the points of intersection, or these may fill the entire cell and lie on the nucleus. The granules take a deep chromatin stain and have basic properties. The cells are occasionally free from granules and then vacuoles are found in the network.

Figure 11.—Türk's Irritation Forms. Magnification 750

These cells are only found in pathological blood after leucocytoses and inflammatory processes. They resemble the large lymphocytes in type, have a large nucleus poor in chromatin, and frequently small nucleoli. The nucleus is not always in the center of the cell and is surrounded by a band of protoplasm which varies in width and takes a dark blue stain. Vacuoles may be found in the cell body. Amitotic nuclear division figures are not uncommon.

Plate V. Figs. 9, 10, 11





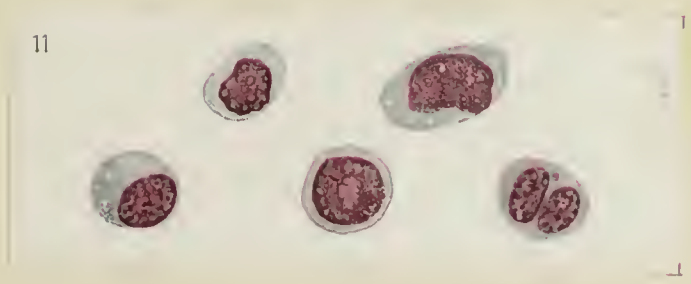


PLATE VI

Figure 12.—Two Eosinophiles and Two Transitionals

Figure 13.—Two Transitionals and Two Basophiles

Figures 12 to 14 show some of the above described leucocytes, as well as a comparison in appearance and size between one another, and the erythrocytes.

Figure 12.—Two Eosinophiles and Two Transitionals. Magnification 750

In the eosinophiles, the characteristic configuration of the nucleus and the arrangement of the distinctly stained granules are particularly evident. The two transitionals present characteristics by means of which they are easily distinguished from polymorphonuclear neutrophiles (see Fig. 6). A few blood platelets are seen on the left.

Figure 13.—Two Transitionals and Two Basophiles. Magnification 750

The upper transitional appears as a large mononuclear leucocyte. Close inspection shows an indented and constricted nucleus. The lower transitional has a lobular nucleus and is probably a more mature cell.

Two basophiles are seen on the right with differently shaped nuclei and coarsely granular protoplasm.


12


13

PLATE VII

Figure 14.—Lymphocytes

Figure 15.—Degeneration Forms of Leucocytes

Figure 14.—Lymphocytes. Magnification 750

The lymphocytes shown in the picture represent an infrequently observed type, and may occasion diagnostic difficulty. The two upper cells illustrate the maximum size of the usually much smaller lymphocyte. The nuclei are poor in chromatin and show distinct nucleoli. The acidophilic granules are well brought out by the *Romanowsky* stain in all three of the cells.

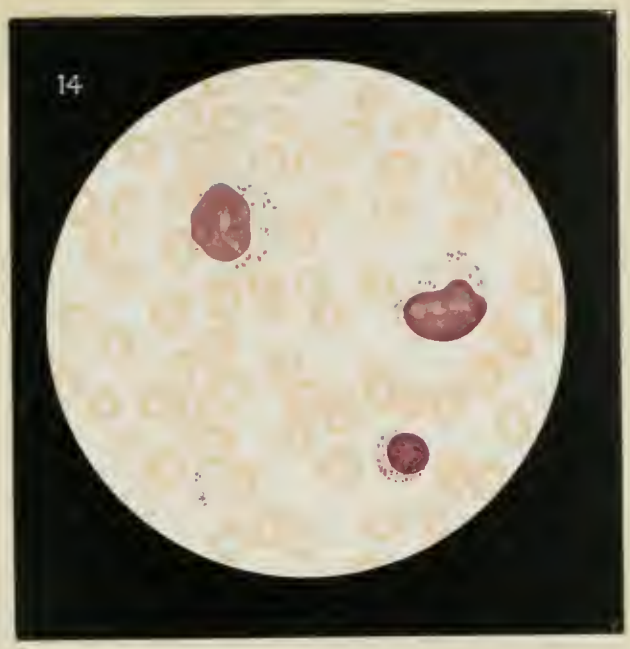
Figure 15.—Degeneration Forms of Leucocytes. Magnification 750

Two neutrophiles are seen above, two lymphocytes to the left, a transitional below, a *Türk's* irritation form on the right and an eosinophile in the center.

All these cells show vacuoles varying in size and number. These changes are usually noted in specimens from much debilitated or moribund patients many hours before death. One of the polymorphonuclear neutrophiles in the picture has been distended, and finally ruptured by the increase in size of the vacuoles.

In the transitional, the zonal stain and the marginal arrangement of the vacuoles are noteworthy, and probably due to lessened resistance at the periphery of the protoplasm.

The occurrence of this vacuolar degeneration in a large number of leucocytes would thus seem to be a bad prognostic sign.


14


15

THE LEUCOCYTOSES

PLATES VIII-XIII FIGURES 16-23

PLATE VIII

Figure 16.—Neutrophilic Leucocytosis

Neutrophilic Leucoeytosis. The diagnosis of this condition is based not only on an increase in the *relative* percentage of polymorphonuclear neutrophiles in the differential count but also on an absolute increase as well. The lowest figures which constitute a neutrophilic leucocytosis are approximately 8,000 neutrophiles in 1 c.mm. the total leucocyte count being about 10,000. The maximum figures are indefinite, but counts over 60,000 neutrophiles in 1 c.mm. are rare. This is the most common type of leucocytosis. The lymphocytes and eosinophiles are usually decreased both in relative percentage and in absolute numbers.

Female, 16 years old. Pleurisy and Exudative Pericarditis. Leucocytes, 34,200 in 1 c.mm.

Figure 16.—Neutrophilic Leucocytosis. Moist Double Cover-glass Specimen. Magnification 750

The erythrocytes are normal in appearance. The white corpuscles, relatively increased in number as compared to the erythrocytes, are seen to be large polymorphonuclear cells with finely granulated protoplasm, indicating that they are polymorphonuclear neutrophiles. Some show ameboid motion.

Plate VIII. Fig. 16

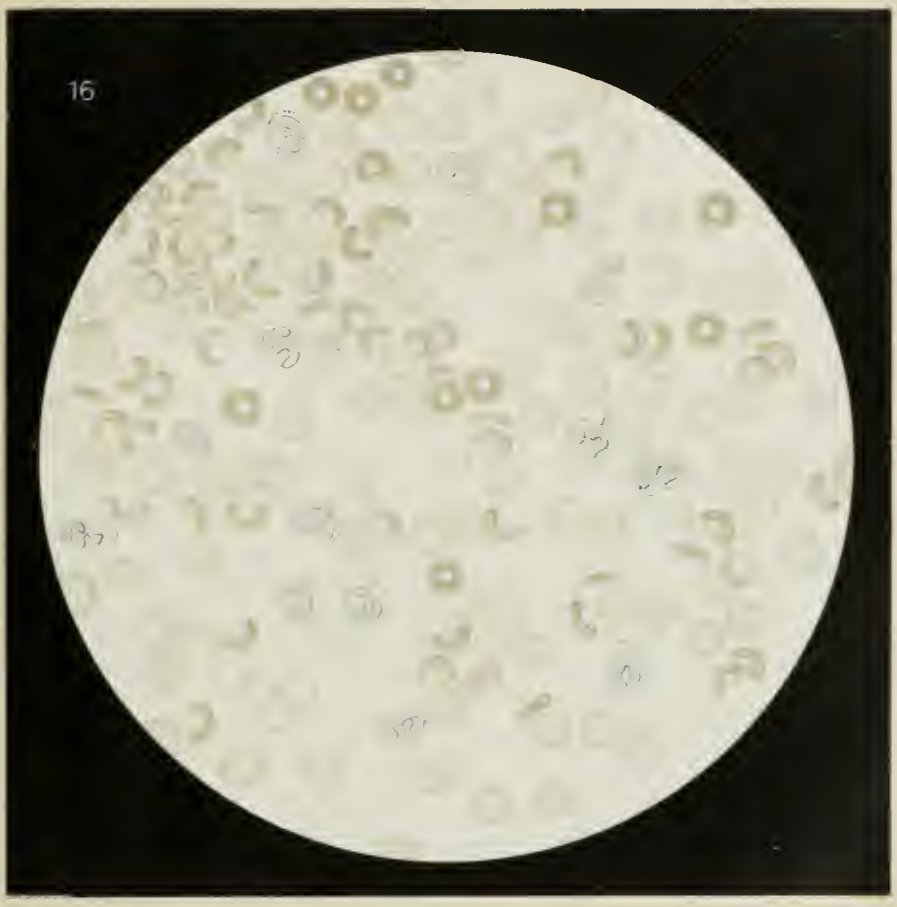


PLATE IX

Figure 17.—Neutrophilic Leucocytosis

The same case.

Figure 17.—Neutrophilic Leucocytosis. Stained Film. Magnification 330

The red corpuscles show slight variations in color due to the slight anemia. Sixteen polymorphonuclear neutrophiles and one transitional are seen in the field. The blood platelets are somewhat increased in number.

Plate IX. Fig. 17

PLATE X

Figure 18.—Eosinophilic Leucocytosis

Eosinophilic Leucocytosis. The increase in the number of eosinophiles in this type of leucocytosis is relatively less marked than the increase of neutrophiles in neutrophilic leucocytosis and corresponds approximately to the relative proportions in normal blood in which there are about 150 to 300 eosinophiles in 1 c.mm. The presence of 6 per cent. or more eosinophiles in the differential count constitutes an eosinophilia when the absolute count is correspondingly increased. This condition is noted chiefly in bronchial asthma, skin disease, helminthiasis and particularly in trichinosis.

Male, 31 years old. Trichinosis. Total leucocyte count 18,000 in c.mm. Differential count shows 49.6 per cent. eosinophiles or 8,930 in 1 c.mm.

Figure 18.—Eosinophilic Leucocytosis. Stained Film. Magnification 330

Erythrocytes unchanged. Numerous leucocytes are seen in the field, the majority (17) of which are eosinophiles, which are easily identified though the granular stain is imperfect. Four neutrophiles are seen in the center and above these there are two lymphocytes and one transitional.

Plate X. Fig. 18

PLATE XI

Figure 19.—Neutrophilic Leucocytosis
Figure 20.—Eosinophilic Leucocytosis

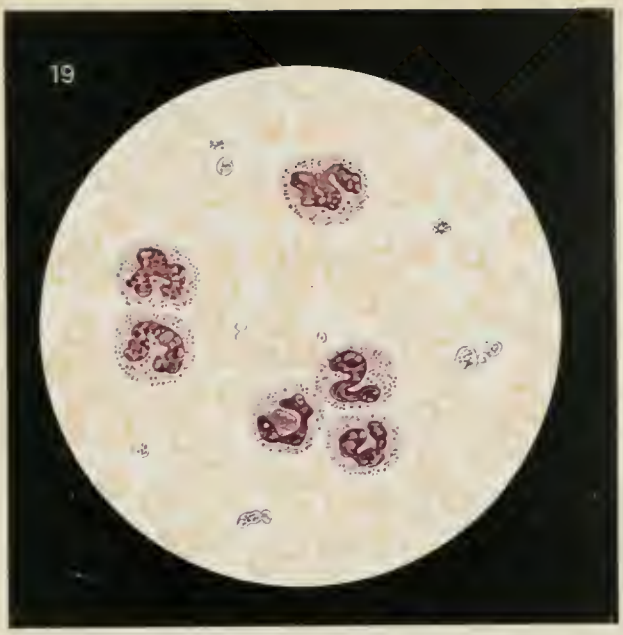
Figure 19.—Neutrophilic Leucocytosis. Stained Film. Magnification 750

The polymorphonuclear type of the cells indicates that they are neutrophiles. The granulation of the protoplasm is denser than in normal blood, a change usually noted in leucocytosis. The blood platelets vary in size and are increased in number.

The same case as Figure 18.

Figure 20.—Eosinophilic Leucocytosis. Stained Film. Magnification 750

The decided increase in the number of eosinophiles is evident. The cells are somewhat smaller than the usual eosinophile, and some show granulations on the nucleus.


19

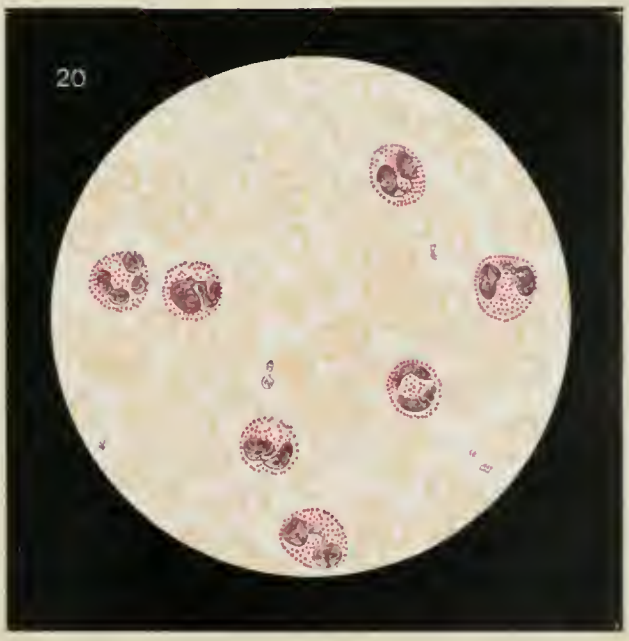

20

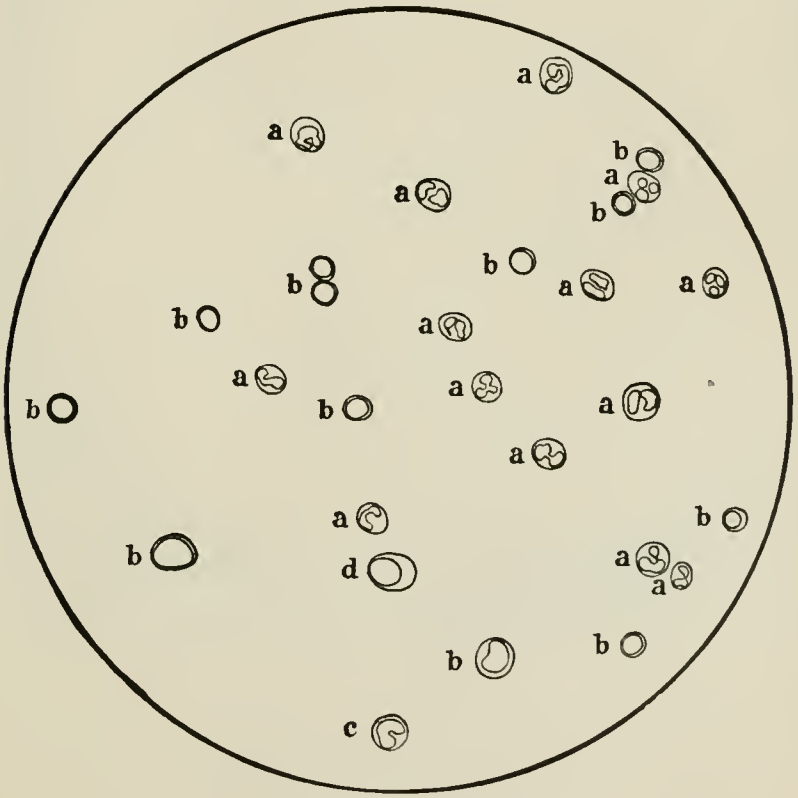
PLATE XII

Figure 21.—The Leucocytosis of Children

Girl, 3 years old. Chronic intestinal catarrh. Leucocytes 14,000 in 1 c.mm. Differential count shows 48 per cent. lymphocytes or 6,500 in 1 c.mm.

Figure 21.—Leucocytosis in a Child. Stained Film. Magnification 330

While a true neutrophilic leucocytosis may occur in children, the simultaneous increase in neutrophiles



a. Polymorphonuclear Neutrophiles.
b. Lymphocytes.
c. Transitionals.
d. *Türk's* irritation forms.

and in mononuclear forms particularly the lymphocytes, is the most frequent type of leucocytosis.

Atypical forms of leucocytes are frequently seen in these cases, such as neutrophiles with round nuclei, *Türk's* irritation forms, and myelocytes, their number serving as an index to the gravity of the disease. The red corpuscles show no particular change.

Plate XII. Fig. 21

PLATE XIII

Figure 22.—Blood Changes in Diphtheria
Figure 23.—Lymphocytosis

Child, 6 years old. Septic diphtheria of nose, fauces and larynx. Duration 8 days. Cutaneous hemorrhages. Blood examination 6 hours before death shows: Hemoglobin, 100 per cent.; red cells, 4,388,000; leucocytes, 72,000.

Figure 22.—Stained Film. Magnification 750

In fatal cases of diphtheria in addition to the usual neutrophilic leucocytosis, numerous neutrophilic myelocytes are found, while these are not noted in favorable cases. *Türk's* irritation forms and mononuclear neutrophiles also may occur in the favorable cases, and have no particular significance, but the presence of myelocytes must always be regarded as an unfavorable prognostic sign.

Six neutrophilic leucocytes are seen in the field; to the right there is a small lymphocyte with scarcely visible protoplasm, toward the center a distorted transitional, and adjoining this there are two neutrophilic myelocytes, their irregular outline due to pressure. The red corpuscles show evidences of some anemia.

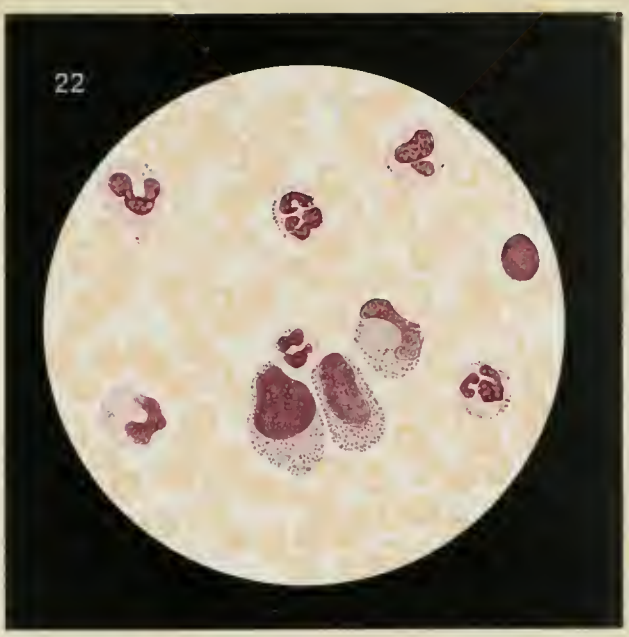
Male, 22 years old. Typhoid fever. 26th day. Hemoglobin, 80 per cent.: red cells, 4,510,000; leucocytes, 6,300. Differential Count: Neutrophiles, 38.5 per cent. or 2,400; lymphocytes, 53.8 per cent. or 3,400; transitionals, 5 per cent.; eosinophiles, 2.4 per cent.; basophiles, none; irritation forms, 0.3 per cent.

Figure 23.—Lymphocytosis. Stained Film. Magnification 750

Lymphocytosis consists of an increase in the relative percentage as well as in the actual number of normal lymphocytes, which are derived in large numbers

from lymph glands by virtue of pathological change or stimulus. The condition is observed in whooping cough, rickets, syphilis and typhoid convalescence, and follows injections of tuberculin.

In the illustration, the red cells show pale centers owing to diminished hemoglobin. Three lymphocytes, and one neutrophile practically without granules, are seen in the field. The lymphocytes all belong to the large type, and one shows slight acidophilic granulation of its protoplasm.


22


23

THE RED CORPUSCLES
OF
THE HUMAN BLOOD
AND
THE BLOOD PLATELETS

PLATE XIV FIGURES 24-26

PLATE XIV

Figure 24.—Erythrocytes

Figure 25.—Erythroblasts

Figure 26.—Blood Platelets

Figure 24.—Erythrocytes. Magnification 750

Normal Erythrocytes are round disks with an average diameter of 7 to 7½ microns, the margin often staining deeper than the center.

Microcytes are abnormally small erythrocytes, round or deformed, with a normal or pale hemoglobin tint. They are to be considered degeneration forms.

Macrocytes are abnormally large erythroeytes, usually quite round, frequently polyehromatophilie, and rarely showing a uniform hemoglobin tint. They represent preliminary stages of the normal erythrocyte.

Poikilocytes are deformed erythroeytes, usually bottle or pear shaped, and often very irregular. The hemoglobin content is always more or less diminished. They are considered degeneration forms which have lost their normal contour on account of lessened resistance.

Figure 25.—Nucleated Red Corpuscles (Erythroblasts). Magnification 750

Erythroblasts represent preliminary stages of normal red blood cells, their appearance in the peripheral blood indieating inereased activity of the bone marrow in the formation of erythroeytes.

Normoblasts are of the same size as erythroeytes and have a relatively large round nucleus showing radiating or segmented structure. The cell body of the mature normoblast has a pure hemoglobin tint, but the younger cells are frequently polyehromatophilie.

Microblasts are characterized by their small size, and show degenerative changes of the cell body (poikilocytosis), and pycnotic nuclei of dense structure, which stain deeply. Free microblast nuclei are sometimes seen, and are easily differentiated from other structures by their small size and dark blue color.

Megaloblasts are two or three times the size of normoblasts, and the older forms have a relatively small nucleus. Polychromatophilic megaloblasts are not uncommon, and present large, loose structured nuclei, poor in chromatin. The megaloblast originates from a pathologically altered regeneration of the blood with a reversion to the embryonic type.

Nuclear Division Figures of Erythroblasts. Amitotic (direct) division is more frequently observed in megaloblasts than in normoblasts. Attention to the hemoglobin or polychromatophilic stain of the cell body differentiates these cells from lymphocytes of similar appearance, in which the nucleus may also undergo amitotic division, but the cell body is always basophilic (blue).

Mitotic division is rarely observed in the leukemias and in pernicious anemia. The nuclear division figures are often large and beautifully marked with more or less distinct diaster formation. The cell body is still slightly basophilic and usually shows basophilic granulation.

Figure 26.—Blood Platelets. Magnification 750

These are blood elements of various shapes, which range in size from some scarcely visible, to others with a diameter of 10 microns. The smallest forms appear as pale, sharply circumscribed disks, which may have crenated margins, and show a nuclear substance also varying in size and often with only few chromatin granules.

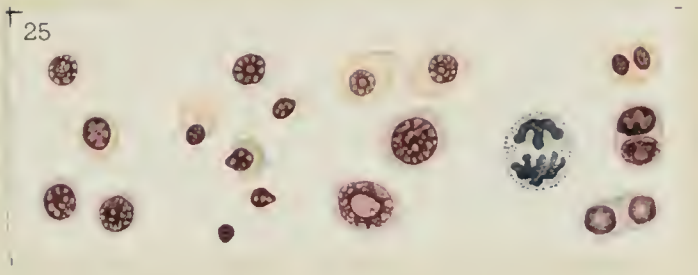
The larger forms are oval or rod-shaped, with abundant nuclear substance of a dark chromatin tint. These may show processes varying in length up to twice the diameter of the platelet, which also contain chromatin (see Fig. 40).

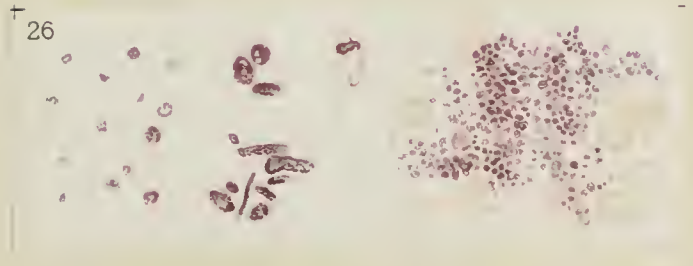
Ordinarily, the platelets occur in small groups, or singly, but in the blood of persons having malignant tumors they may be found aggregated in large numbers.

The origin and the significance of the platelets are still obscure. They are usually found increased in number during, and after, all conditions associated with leucocytosis, or with disintegration of leucocytes. They are enormously increased in myelogenous leukemia.

The practical method of determining their number is by means of an approximate estimate in the stained film.


24


25


26

THE ANEMIAS

PLATES XV-XXII FIGURES 27-41

PLATES XV-XXII

Figures 27-41.—The Anemias

Polychromatophilia

This term indicates a changed behavior of the erythrocytes toward the stain. Polychromatophilic erythrocytes show a mixed staining quality varying from an almost pure eosin to a dirty blue or violet. In the more marked instances the corpuscles appear spotted as if occupied by a basophilic stroma.

The condition is found in all stages of development of the immature erythrocyte, particularly in the nucleated cells, and those showing nuclear division figures. It is, therefore, regarded as a sign of immaturity of the red corpuscle, and consequently a symptom of increased regeneration.

PLATE XV

Figure 27.—Karyolytic Forms of Erythroblasts

Figure 28.—Polychromatophilic Erythrocytes

Figure 27.—Karyolytic Forms of Erythroblasts. Magnification 750

These are often present in large numbers in cases of progressive severe anemia, and particularly in the anemia of congenital syphilis in children.

The nuclei are extremely varied in appearance and show budding and constrictions with pycnotic segments. A small nucleus, poor in chromatin, is sometimes seen in a polychromatophilic cell, apparently a remnant of an original nucleus which has undergone dissolution.

Child, 2½ years old. Anemia gravis with congenital syphilis. Red cells, 1,564,000; leucocytes, 14,000.

Figure 28.—Polychromatophilic Erythrocytes. Stained Film. Magnification 750

The erythrocytes show moderate variations in size and shape, with both slight and pronounced polychromatophilia (see Fig. 41). A megaloblast in process of division, with polychromatophilic cell body, is seen above, and on the right there is a lymphocyte with the usual blue stained protoplasm.


27


28

PLATE XVI

Figure 29.—Basophilic Granulation

Figure 30.—Lead Poisoning

Basophilic Granulation

In this change the normal erythrocyte, or more frequently the polychromatophilic erythrocyte, contains granules which take a basic stain. The granules vary in size; some are scarcely visible and others are as large as the neutrophilic granules in leucocytes. Poikilocytes and microcytes occasionally contain unusually large angular granules. They also vary in number, sometimes filling the entire cell.

Basophilic granulation is also found in nucleated red cells and in those presenting nuclear division figures. Polychromatophilia being considered an indication of immaturity, the designation of an accompanying basophilic granulation as "granular degeneration" does not seem justified, but as yet no definite opinion is possible. It is observed in all types of anemia and particularly in cases of lead poisoning.

Figure 29.—Basophilic Granulation. Stained Film. Magnification 750

Composite picture of specimens from a case of chronic lead poisoning. The varieties of basophilic granulation and its combination with polychromatophilia are the noteworthy features.

Male, 25 years old. Painter, suffering from chronic lead poisoning.

Figure 30.—Lead Poisoning. Stained Film. Magnification 750

Granular erythrocytes are invariably present in cases of lead poisoning. They are more numerous

in this condition than in any other disease, and the blood picture is practically pathognomonic.

The erythrocytes show slight variations in size and color. In some the color is limited to the margins and slight polychromatophilia is apparent. Nine red cells which have more or less marked basophilic granulation are seen in the field.


29


30

PLATES XVII-XIX

Figures 31-36.—Secondary Anemia

Secondary anemia includes all the anemic conditions developing in the course of different diseases which are not based on the primary involvement of the blood-making organs. The group includes all affections leading to loss of blood, malnutrition and cachexia (gastric and intestinal ulcers, animal parasites, infectious diseases, malignant tumors). In order to study the morphology of the red corpuscles in primary as well as secondary anemia, it is essential to examine fresh specimens, as the changes noted in stained films are often artefacts.

PLATE XVII

Figure 31.—Acute Anemia

Figure 32.—Chronic Anemia

Secondary Anemia. Acute Form

Soon after a severe hemorrhage there is a diminution in the number of red corpuscles and in the amount of hemoglobin, due to a transfer of fluids from the tissues into the blood. Regenerative phenomena are soon noted by the presence of polychromatophilia, macrocytes and normoblasts, which immature forms are usually deficient in hemoglobin. The number of red cells increases rapidly, while the increase in hemoglobin content is slower.

Female, 45 years old. Ulcer of the stomach. Hemoglobin, 35 per cent.; red corpuscles, 1,960,000; leucocytes, 6,300 in 1 c.mm.

Figure 31.—Acute Anemia. Stained Film. Magnification 750

The erythrocytes are further apart in the stained specimen, owing to the dilution of the blood. The lack of uniformity in size is due to the presence of numerous polychromatophilic macrocytes, and not to changes in the normal cells. A polychromatophilic normoblast is seen above and a lymphocyte below. Several blood platelets are also present.

Secondary Anemia. Chronic Form

In addition to the changes noted above, these cases also show variations in the shape of the red cells and a more or less pronounced diminution in the amount of hemoglobin. The red cells may simply show decided loss of hemoglobin, without polychromatophilia. An absence of immature erythrocytes in cases of secondary anemia justifies a suspicion of

paralysis of function of the bone marrow, as far as formation of erythrocytes is concerned. The more numerous the immature red cells, the greater the functional activity of the blood-forming organs. When the bone marrow is suddenly called upon to supply a marked deficit, there may be a transitory flooding of the circulation with many nucleated cells.

Male, 54 years old. Carcinoma of stomach. Hemoglobin, 35 per cent.; red cells, 1,336,000; leucocytes, 13,100 in 1 c.mm.

Figure 32.—Chronic Anemia. Stained Film. Magnification 750

The red cells show the characteristic evidences of secondary anemia, *i.e.*, diminished and uneven hemoglobin distribution, polychromatophilia, changes in size and shape of corpuscles.


31

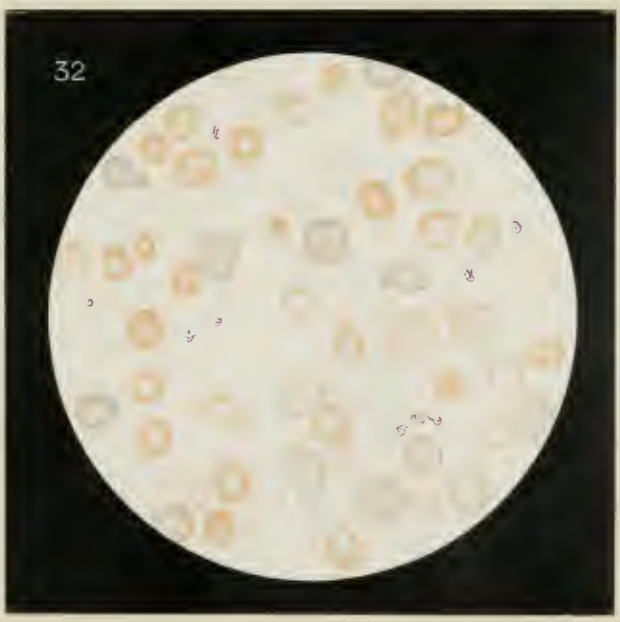

32

PLATE XVIII

Figure 33.—Chronic Anemia
Figure 34.—Infantile Hereditary Syphilis

Figure 33.—Chronic Anemia. Stained Film. Magnification 330

The same changes are noted as in Fig. 32, and the pathological condition is particularly apparent when compared with Fig. 3, which represents normal blood.

Two neutrophiles are seen in the field, with a normoblast above and numerous blood platelets.

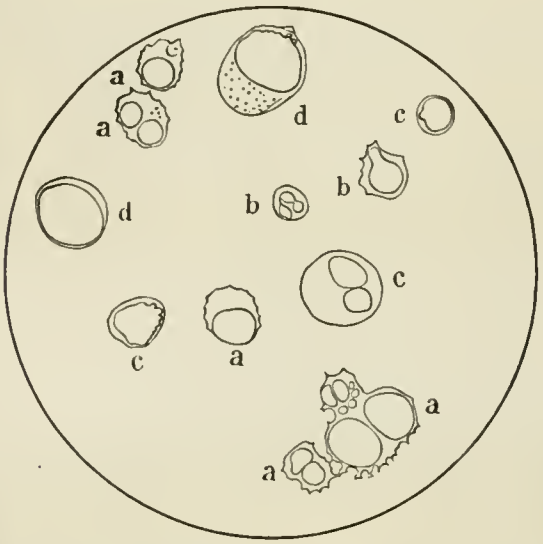
Anemia in Children having Congenital Syphilis

In well marked cases the changes in the red cells are sufficiently pronounced to make this one of the cardinal symptoms. In addition to a leucocytosis, numerous bone-marrow cells are found, which justify the belief that the bones are also involved in the pathological lesion and that the presence of these cells is the result of direct irritation of the bone marrow by the local syphilitic process. Neutrophilic and eosinophilic myelocytes and immature lymphocytes are present, together with a large number of nucleated red cells, microblasts, normoblasts and frequently megaloblasts and nuclear division figures. The large number of karyolytic forms is noteworthy (see Fig. 27). The red cells appear deficient in pigment, but poikilocytosis, polychromatophilia, and basophilic granulation are not common. The number of erythrocytes is always considerably diminished, with a corresponding reduction in the amount of hemoglobin.

Child, 1½ years old. Hereditary syphilis. Red cells, 2,500,000; leucocytes, 18,000 in 1 c.mm.

Figure 34.—Infantile Hereditary Syphilis. Stained Film. Magnification 750

The specimen contained numerous nucleated red cells their number exceeding the total leucocyte count. The stained film of blood, obtained after death, shows some disintegrating cells.



a. Normoblasts and Megaloblasts. Some of the latter unusually large, with more or less basophilic protoplasm, and one or more nuclei poor in chromatin.
b. Karyolytic Forms of Normoblasts and Megaloblasts.
c. Lymphocytes. One with divided Nucleus.
d. Granular and Non-granular Bone marrow Cells.


33

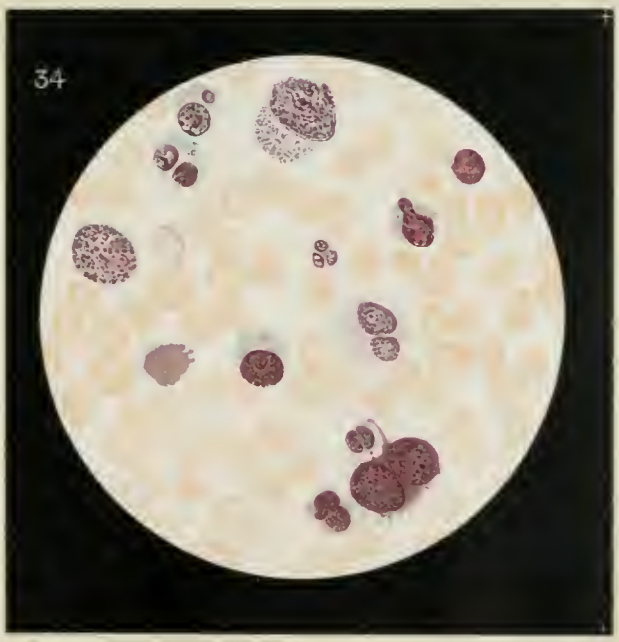

34

PLATE XIX

Figure 35.—Secondary Anemia. Chronic Form

Figure 36.—Crenated Red Corpuscles

Secondary Anemias

Same case as Figure 32.

Figure 35.—Chronic Secondary Anemia. Fresh Double Cover-glass Specimen. Magnification 750

The pale tint of the red cells indicates their loss of hemoglobin, especially when compared with normal blood.

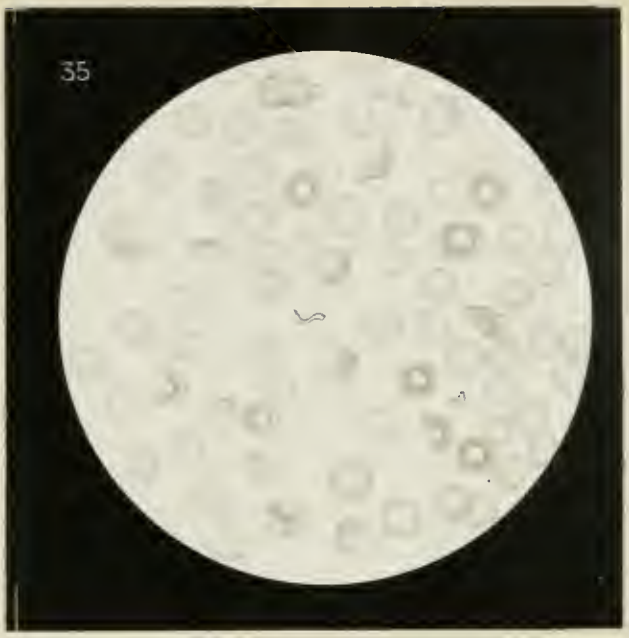
The varied outline of red corpuscles is most apparent in the fresh specimen, but an opinion as to their size requires experience. Pear-shaped and bottle-shaped cells, and multilobular poikilocytes are present. A microcyte is seen in the center of the field. The two humped and oblong red cells are changes, due presumably to evaporation, the details of which are seen in the following picture.

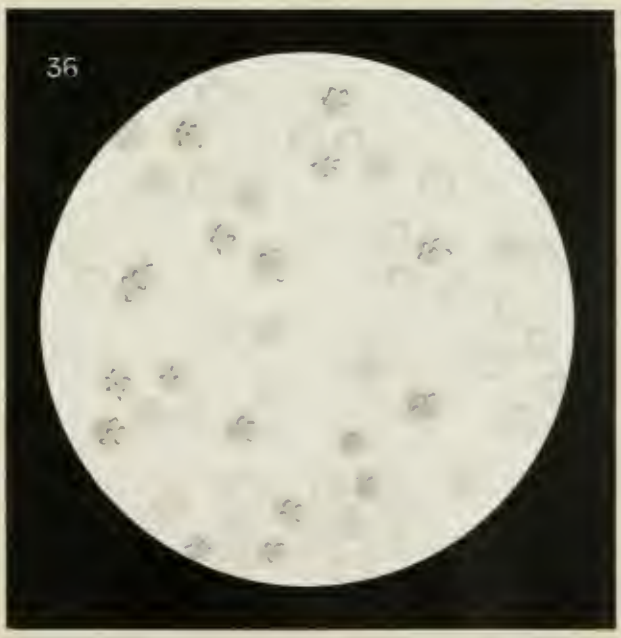
Figure 36.—Crenated Erythrocytes. Fresh Double Cover-glass Specimen. Magnification 750

The illustration shows the crenated forms of red cells, formerly believed to be the same thing as poikilocytes. The characteristic changes are evident.

The crenated forms may be observed in any specimen of fresh blood which has evaporated or suffered mechanical injury. In fact the occurrence of a few of these near the margin can scarcely be prevented in the fresh specimens, though carefully prepared.

Crenation within a few seconds of all the red corpuscles in a properly made specimen is pathological, and must be considered an evidence of lessened resistance on the part of the erythrocytes. Error is prevented by observing this in several successively prepared specimens. Normal blood does not show this change to any extent until after the lapse of from thirty minutes to several hours.


35


36

PLATES XX-XXII

Figures 37-41.—Primary Anemias

The Primary Anemias

The characteristic feature in the diagnosis of primary anemia, is the presence of anemic conditions, varying in kind and degree, with an absence of all other causative diseases. In chlorosis and certain anemias of childhood, nothing but an affection of the blood itself has as yet been demonstrated, whereas in pernicious anemia the blood-forming organs are the seat of the lesion.

The anemias of childhood present no specific or particularly characteristic changes in the blood, but in chlorosis, as well as in pernicious anemia, definite evidences are found, which are characteristic of the one or the other condition.

PLATE XX

Figure 37.—Pernicious Anemia
Figure 38.—Chlorosis

Female, 63 years old. Pernicious Anemia. Hemoglobin, 35 per cent.; red cells, 1,032,000; leucocytes, 16,000 in 1 c.mm. Marked polychromatophilia and pronounced variations in the size of the red cells. Normoblasts and megaloblasts are present.

Figure 37.— Pernicious Anemia. Fresh Double Cover-glass Specimen. Magnification 750

Most of the red cells are deficient in hemoglobin, but some have a normal color. The uneven distribution of hemoglobin is always apparent. The pronounced difference in the size of the corpuscles is noteworthy; about half of them are megalocytes, and there are also many microcytes, some so small that they are difficult to distinguish from blood platelets in the fresh specimen.

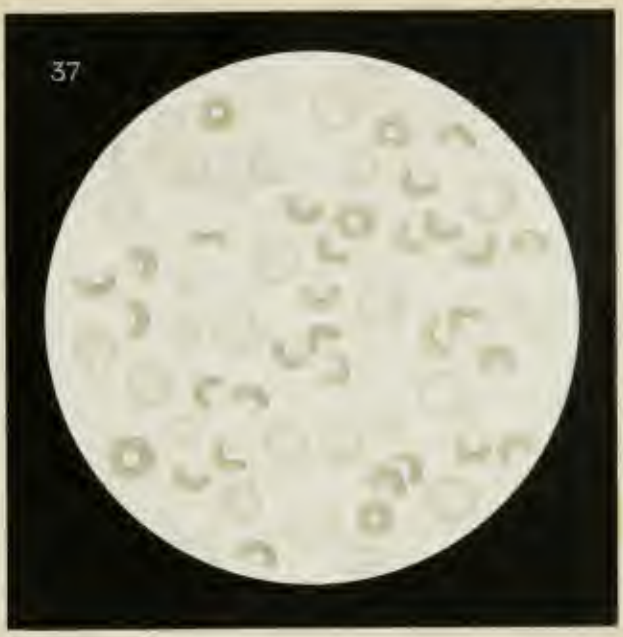
Poikilocytosis was not a pronounced feature in this case of pernicious anemia in which the diagnosis was verified by autopsy. This change is evidently not present to the same degree in every case, and probably depends to some extent on the duration of the disease.

Female, 28 years old. Chlorosis. Hemoglobin, 50 per cent.; red cells, 4,320,000; leucocytes, 9,600 in 1 c.mm.

Figure 38.—Chlorosis. Fresh Double Coverglass Specimen. Magnification 750

In chlorosis, even the fresh blood differs in several essential features from that of secondary anemia or of pernicious anemia. Primarily, the erythrocytes show a uniform decided diminution in blood-coloring matter, which is very apparent in severe cases. Poikilocytosis is not as pronounced in severe chlorosis as it is in severe secondary anemia, and the marked difference in the size of the corpuscles seen in pernicious anemia, is absent. In cases of severe hydremia a uniform increase in the size of a large number of erythrocytes is frequently observed. When the chlorosis is not pronounced, no particularly characteristic changes can be made out in a fresh specimen.

Figure 38 shows a specimen of blood from a case of chlorosis. The red cells are practically uniform in size and very pale in color. Few pear-shaped poikilocytes are present. The erythrocytes, viewed laterally, show a light zone which is probably a reflection.


37


38

PLATE XXI

Figures 39-40.—Chlorosis.

Girl, 26 years old. Severe Chlorosis. Hemoglobin, 35 per cent.; red cells, 4,000,000; lymphocytes, 4,400 in 1 c.mm.

Figure 39.—Chlorosis. Stained Film. Magnification 750

In chlorosis the diminution in the amount of hemoglobin is much greater than in the number of red corpuscles, and this characteristic loss of coloring matter is apparent in all the corpuscles by the narrow stained rim as shown in the illustration. There is only a slight difference in the size of the cells, but poikilocytosis is evident. The platelets are increased in number. A lymphocyte is seen on the right.

Female, 26 years old. Convalescing Chlorosis. Hemoglobin, 90 per cent.; red cells, 4,600,000; leucocytes, 7,200 in 1 c.mm.

Figure 40.—Chlorosis. Stained Film. Magnification 750

The specimen shows the decided and uniform increase in the amount of hemoglobin in the corpuscles during convalescence, but the pale centers indicate that this is not yet quite normal. Few poikilocytes are present.

The flagella-like processes of the platelets are seen in this specimen.


39

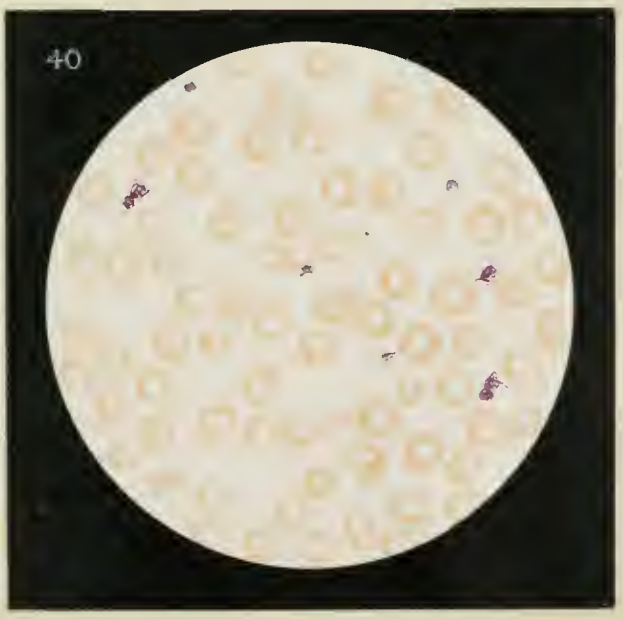

40

PLATE XXII

Figure 41.—Pernicious Anemia

Pernicious Anemia

In cases of pernicious anemia the blood as a rule presents a characteristic series of changes not noted in any other disease. The diminution in the number of red corpuscles is out of proportion to the loss of hemoglobin. In making the red cell count, care should be exercised not to overlook the numerous microcytes usually present. The disproportionate loss of red cells and hemoglobin is explained by the fact that, while very pale corpuscles are seen, there are also many which contain a normal amount of blood pigment. Decided polychromatophilia is invariably noted, and basophilic granulation is common. Pronounced poikilocytosis seems to develop only in the protracted cases. The presence of megalocytes and megaloblasts constitutes a particularly characteristic feature, and their occurrence is explained by a megaloblastic transformation of the bone marrow as far as the formation of red cells is concerned. Mitoses of erythroblasts may also be found. These evidences of disintegration and abnormal regeneration of the blood are not found in chlorosis or secondary anemia.

The leucocyte count in pernicious anemia varies considerably. Leucopenia is an unfavorable prognostic sign. While neutrophilic leucocytosis is noted in the course of improvement, it may also be indicative of inflammatory complications. The presence of myelocytes and *Türk's* irritation forms is not uncommon.

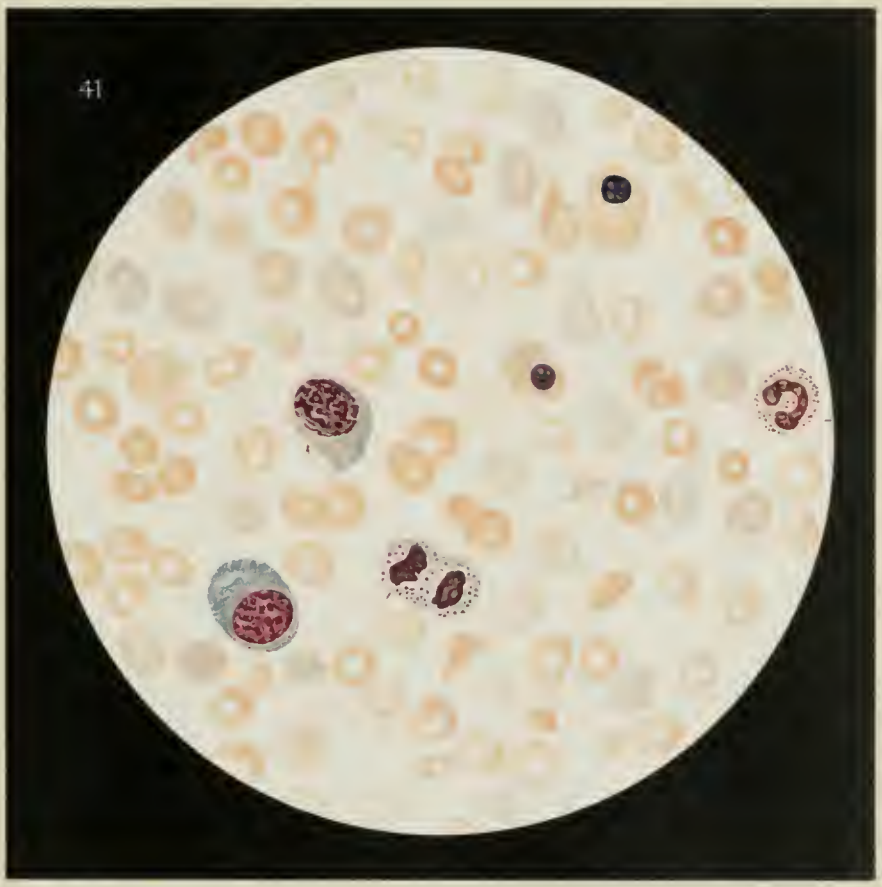
Same case as Figure 37. Duration of disease four weeks.

Figure 41.—Pernicious Anemia. Stained Film. Magnification 750

The decided polychromatophilia and the slight poikilocytosis are apparent and probably explained by the severity and short duration of the case. Lack of uniformity in the distribution of hemoglobin is also evident, some cells being very pale, while others seem to contain an excessive amount of blood pigment.

Two megaloblasts with pyenotic nuclei are seen above, to the right, and in the center there is a megaloblast with a large nucleus poor in chromatin and a basophilic cell body. A *Türk's* irritation form is seen immediately beneath the latter, and these two cells show a striking resemblance. A megaloblast in process of mitotic division is also seen, and to the right a polymorphonuclear neutrophile.

Plate XXII. Fig. 41



THE LEUKEMIAS

PLATES XXIII-XXXVII FIGURES 42-58

PLATES XXIII-XXXVII

Figures 42-58.—The Leukemias

The Leukemias

The diagnosis of leukemia is based on the demonstration of a permanent increase in the number of white corpuscles in the blood, a large percentage of which are bone marrow cells or abnormal leucocytes. This statement applies to myelogenous leukemia as well as to lymphatic leukemia, and for the present this classification seems desirable, as it is based on the condition of the blood. Further subdivisions do not seem indicated as yet, particularly as almost every case of leukemia presents individual characteristics. These may undergo pronounced change in the course of the disease, by variations in the relative proportion of the different varieties of cells, as well as by the disappearance of some and sudden appearance of other types.

All cases show a more or less marked anemia, which may present all the characteristics of a pernicious anemia, but some are seen, with several hundred thousand leucocytes in a cubic millimeter, without apparent change in the red cells. The severity of the disease is appreciably dependent on the condition of the red cells.

A detailed description of the changes in the blood in the different forms of leukemia will be found in connection with the following illustrations.

PLATE XXIII

Figure 42.—Myelogenous Leukemia

Female, 23 years old. Myelogenous Leukemia. Hemoglobin, 65 per cent.; red cells, 3,200,000; leucocytes, 337,000 in 1 c.mm.

Figure 42.—Myelogenous Leukemia. Fresh Double Cover-glass Specimen. Magnification 750

The decided increase in the number of leucocytes is evident. In this connection it is well to recall that some cases of leukemia may show comparatively low leucocyte counts, for example, 10,000 in 1 c.mm., whereas a leucocytosis of 50,000 or more may exist for a considerable period. Consequently the count alone is not sufficient for diagnosis. As considerable practice is necessary to differentiate the various types of leucocytes in a fresh unstained specimen, and some cannot be recognized in this way at all, the dried and stained films are preferable for the purpose.

The red cells show no essential change. The following four types of leucocytes can be recognized in the illustration:

a. Polymorphonuclear finely granular forms, noted in Fig. 16, are neutrophiles.

b. Cells of the same size with round or lobulated nuclei and coarse refractive granulation are eosinophilic myelocytes or eosinophiles.

c. Larger and lighter cells with round nuclei and finely granular protoplasm are bone marrow cells, which can be more accurately classified in the stained specimen.

d. Small leucocytes of different forms which also cannot be classified in the unstained specimens.

The greater the variety of leucocytes present, the more difficult the classification, in unstained specimens.

Plate XXIII. Fig. 42

PLATE XXIV

Figures 43-44.—Myelogenous Leukemia

Male, 62 years old. Myelogenous Leukemia. Blood very concentrated. Hemoglobin, 105 per cent.: red cells, 5,184,000; leucocytes, 59,300 in 1 c.mm.

Figure 43.—Myelogenous Leukemia. Fresh Double Cover-glass Specimen. Magnification 750

The addition of a few drops of an aqueous solution of gentian violet to the diluting fluid differentiates the leucocytes somewhat (compare Fig. 42), but is not sufficient for the proper classification and recognition of the pathological forms. The red cells show but little change in shape and size. A group of blood platelets is seen in the center, on the right a polymorphonuclear neutrophile, on the left two granular bone-marrow cells and above a lymphocyte.

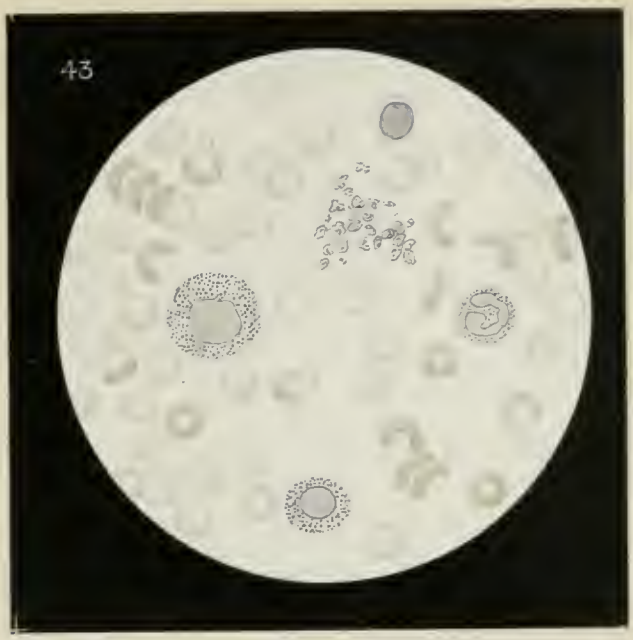
The same case.

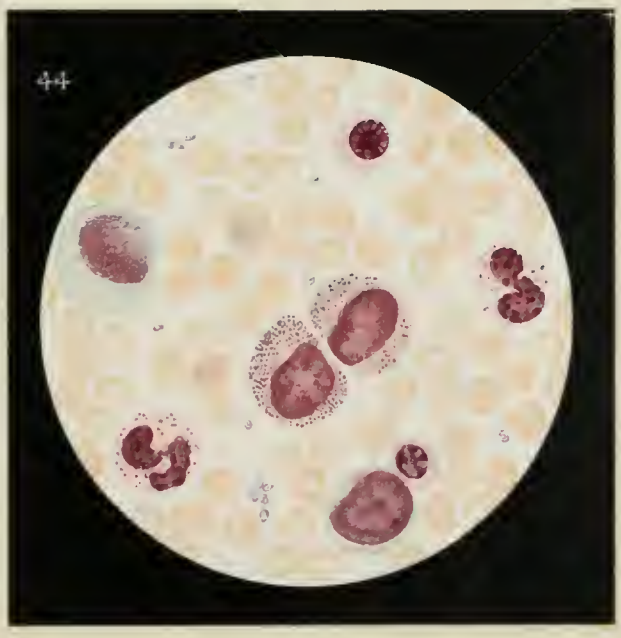
Figure 44.—Myelogenous Leukemia. Stained Film. Magnification 750

The various characteristics of the different varieties of leucocytes are apparent in the stained specimen. In the fresh specimen, for example, it is impossible to distinguish the neutrophilic myelocyte from the basophilic mononuclear, as the vesicular structure of the latter looks just like the fine granulation of the former.

The red cells show evidence of considerable anemia. While undue concentration of the blood has given normal hemoglobin and red cell figures as above, the anemic changes of the red cells are made apparent in the stained specimen by differences in size, irregu-

larity in shape, polychromatophilia and the presence of normoblasts. A megaloblast is seen above and a normoblast below, both showing polychromatophilia. Two polymorphonuclear neutrophiles and blood platelets are also present. The other cells will be described later.


43


44

PLATES XXV-XXVIII

Figures 45-49.—Chronic Lymphatic Leukemia

Chronic Lymphatic Leukemia

Chronic lymphatic leukemia is characterized by the presence in the blood of varying numbers of abnormal lymphocytes, usually of the small, but occasionally of the large type. The absolute counts are generally high, ranging from 50,000 to 1,000,000 in 1 c.mm. The relative percentage of these lymphocytes is also high, ranging from 95 to 99 per cent. of the leucocytes, there being an absolute decrease in the other varieties.

The appearance of the blood is not complex, and is absolutely characteristic of the condition.

The red corpuscles are usually in fair condition, and only show extensive change in the advanced and terminal stages of the disease, when there is a decrease in their number and a corresponding loss in the amount of hemoglobin.

The blood platelets are slightly, if at all, increased in numbers.

PLATE XXV

Figure 45.—Chronic Lymphatic Leukemia

Male, 44 years old, sick for one year. Multiple swellings of lymphatic glands. Spleen enlarged, and extending to the median line. Progressive anemia for the past three months. Duration of disease eighteen months.

A complete examination of the blood could not be made, but the stained film justifies a diagnosis of chronic lymphatic leukemia.

Figure 45.—Chronic Lymphatic Leukemia. Stained Film. Magnification 330

The increase in the number of lymphocytes is such that there are more white than red cells. The lymphocytes all appear of approximately the same size and show a very narrow margin of protoplasm, barely visible in some. There are a few somewhat larger lymphocytes with a lighter colored nucleus. An abnormal segmentation of the nuclei is noted which is foreign to lymphocytes in normal blood. (For details see Fig. 47.)

The red cells show no change except diminished hemoglobin content.

Plate XXV. Fig. 45

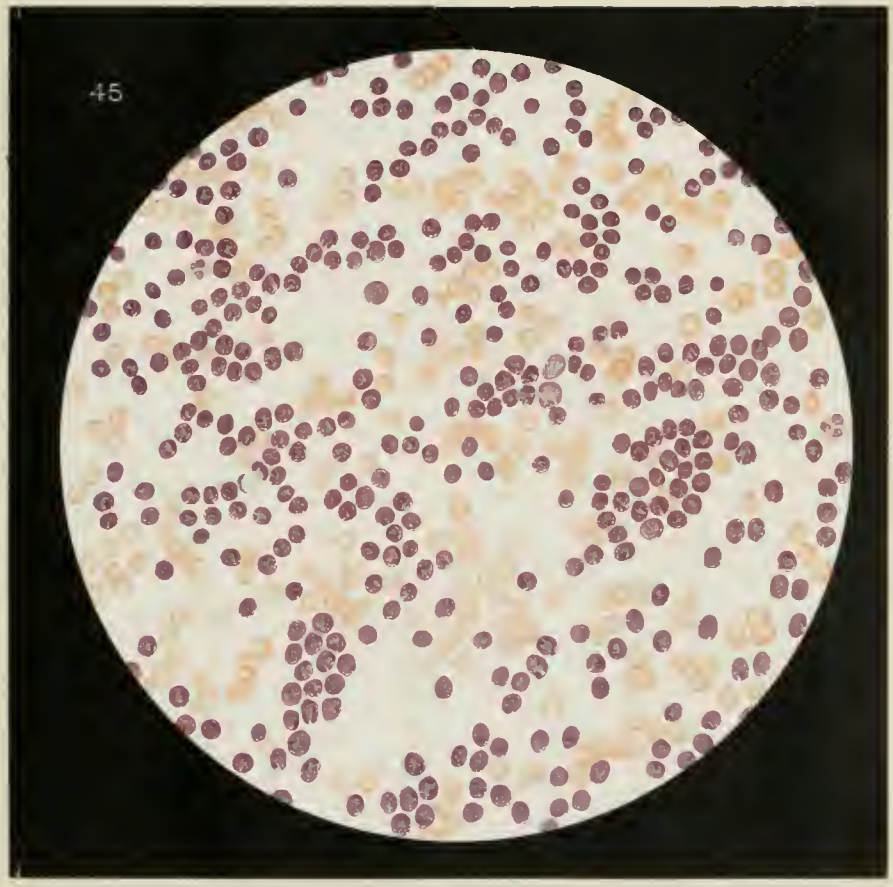


PLATE XXVI

Figures 46-47.—Chronic Lymphatic Leukemia

Chronic Lymphatic Leukemia. For detailed condition of the blood see description of Fig. 48.

Figure 46.—Chronic Lymphatic Leukemia. Fresh Double Cover-glass Specimen. Magnification 750

The nuclei of the lymphocytes are stained light blue by the addition of a drop of aqueous solution of gentian violet to the diluting fluid. Nothing abnormal is apparent in the lymphocytes of this wet specimen, except that they appear a little larger than those in normal blood. A polymorphonuclear neutrophile is seen on the right. The red cells show a normal amount of coloring matter.

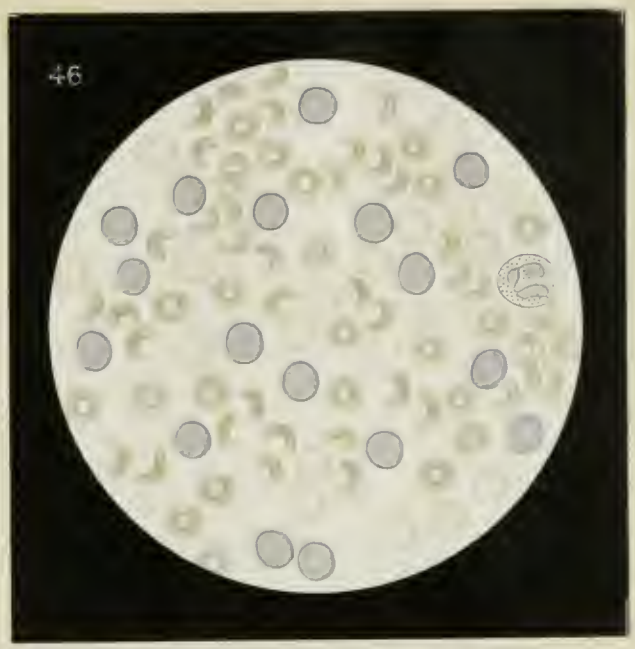
The same specimen as in Fig. 45.

Figure 47.—Chronic Lymphatic Leukemia. Stained Film. Magnification 750

A thin smear is essential in order to recognize the abnormal features of the lymphocytes in chronic lymphatic leukemia, as they differ considerably from the small lymphocytes of normal blood. They are larger and have apparently segmented nuclei, poor in chromatin, which practically fill the cells and lend the impression of immaturity. There is a narrow margin of protoplasm, sometimes barely visible. Acidophilic granules cannot be demonstrated.

These cells must be considered immature lymphocytes representing a definite stage in the development of the lymphocytes of normal blood.

The red corpuscles are somewhat deficient in hemoglobin.


46

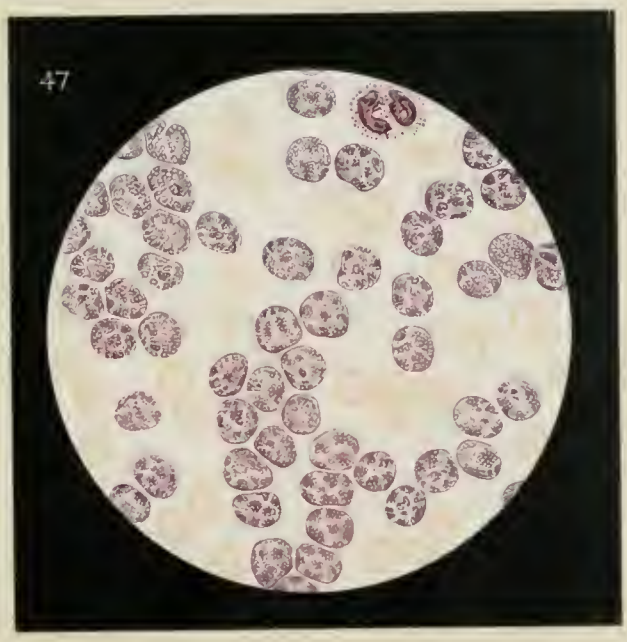

47

PLATE XXVII

Figure 48.—Chronic Lymphatic Leukemia

Male, 38 years old. For past eighteen months progressive glandular swellings in the neck and both axillæ. At present all superficial glands are palpable and about the size of a plum. Spleen 10 × 7 cm. The blood has normal appearance and concentration. Hemoglobin, 115 per cent.; red cells, 4,928,000; leucocytes, 79,000 in 1 c.mm. Differential count: Polymorphonuclear neutrophiles, 5.2 per cent. (4,090); lymphocytes, 94.2 per cent. (74,390); transitionals, 0.4 per cent. (370); eosinophiles, 0.2 per cent. (150).

Diagnosis: Chronic Lymphatic Leukemia.

Figure 48.—Chronic Lymphatic Leukemia. Stained Film. Magnification 330

The increase in the number of lymphocytes is not nearly as great in this case as in Fig. 45. Most of the cells show the characteristics described above. A few of the lymphocytes have a larger amount of protoplasm, and others show an irregular or notched nucleus. On the right is seen a nuclear figure, poor in chromatin, which looks like a flattened nuclear remnant, but really has a different significance, as seen in Fig. 49.

The red cells are practically normal. The platelets are increased in numbers.

Plate XXVII. Fig. 48

PLATE XXVIII

Figure 49.—Chronic Lymphatic Leukemia

Male, 56 years old. During the past four years he has had glandular swellings on both sides of the neck, with periods of remission. Renewed swelling has been present for the past year with the addition of glandular enlargement in both axillæ, in the inguinal folds, near the eyes and at the angle of the jaw. Spleen is considerably enlarged (24 × 16 cm.). Moderate cachexia.

Hemoglobin, 105 per cent.; red cells, 5,176,000; leucocytes, 53,600 in 1 c.mm. Differential count: Polymorphonuclear neutrophiles, 6.2 per cent. or 3,400; lymphocytes, 92.7 per cent. or 50,000, of which 16.5 per cent. or 8,900 are large fragile forms. Transitionals and eosinophiles, 0.55 per cent. each, or 300 each in 1 c.mm.

Diagnosis: Chronic Lymphatic Leukemia.

Figure 49.—Chronic Lymphatic Leukemia. Stained Film. Magnification 750

In addition to the abnormal lymphocytes described above, almost every case of chronic lymphatic leukemia shows fragmentary nuclear structures poor in chromatin. The nucleus often has the appearance of being partially dissolved, and looks like a granular mass devoid of protoplasm. Well preserved cells of this type are rarely seen, justifying the inference that they are very fragile and non-resistant, or that they cannot exist in the peripheral circulation. Some of these resemble large lymphocytes, while others are like large homogeneous, slightly basophilic bone marrow cells. Their nuclei, poor in chromatin, are indented or lobulated, rarely showing nucleoli.

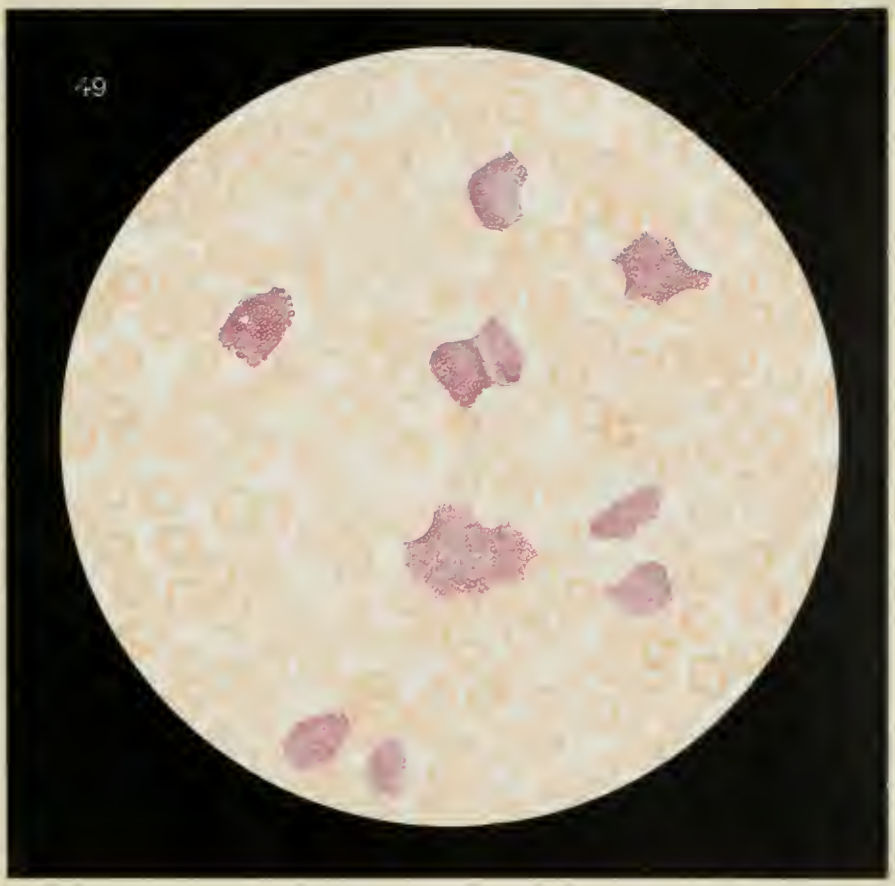
These large cells must be considered as the large homogeneous bone marrow cells which enter the circulation at this stage of their development.

In another case where the ordinary type of small lymphocytes was usually present, the author noted

two short periods during which the blood contained large numbers of these "fragile cells," which would seem to indicate a specific irritation of the bone marrow.

When this large type of cell occurs in chronic lymphatic leukemia, it seems reasonable to conclude that there is also a lesion of the bone marrow.

Plate XXVIII. Fig. 49



PLATES XXIX-XXXV

Figures 50-56.—Myelogenous Leukemia

Myelogenous Leukemia

Contrary to the rather uniform changes in the blood noted in chronic lymphatic leukemia, the cases of myelogenous leukemia present a most varied and sometimes confusing picture. All types of leucocytes found in normal blood are present, in addition to myelocytes in different stages of development. The leucocyte count is always high, ranging usually between 200,000 and 2,000,000, and figures below 50,000 in 1 c.mm. are rare.

The leucocyte count may recede several thousand as the result of intercurrent febrile disorders (sepsis, tuberculosis, etc.), or therapeutic measures (arsenic, X-ray, etc.), but myelocytes are invariably present in the peripheral circulation, even under these circumstances, and the diagnosis of myelogenous leukemia is evident.

While there is an increase in the actual number of each variety, the polymorphonuclear neutrophile is the normal cell to which this applies chiefly. The myelocytes also show high figures, and several hundred thousand may be present in 1 c.mm. One or other type of these bone marrow cells usually predominates during the entire course of the disease, and the different types are rarely present in equal numbers.

The diagnosis of myelogenous leukemia can be made on examination of the blood, even if the leuco-

cyte count is not excessive. In addition to the leucocyte increase, these cases invariably show changes in the red cells which are, however, not as pronounced as in acute leukemia. The blood platelets are always decidedly increased in number.

The seven plates on the following pages illustrate four types of myelogenous leukemia, each characteristic on account of the predominance of special cellular types.

PLATE XXIX

Figure 50.—Myelogenous Leukemia

Female, 25 years old. Has been ill for the past three years, and under treatment for leukemic enlargement of the spleen for two years. Occasional periods of improvement, due to administration of arsenic. On admission to hospital rather pale and emaciated. Has a greatly enlarged spleen extending to the symphysis, and numerous cutaneous thrombi.

The blood is thin and coagulation is retarded. Hemoglobin, 70 per cent.: red cells, 3,300,000; leucocytes, 390,000 in 1 c.mm. Differential count: Neutrophiles, 43.07 per cent., or 168,000; lymphocytes, 1.88 per cent., or 7,000; transitionals, 2.31 per cent., or 9,000; eosinophiles, 3.46 per cent., or 13,500; basophiles, 12.17 per cent., or 47,500; myelocytes, 37.11 per cent., or 145,000 in 1 c.mm.

Diagnosis: Myelogenous Leukemia.

Figure 50.—Myelogenous Leukemia. Stained Film. Magnification 330

The difference between the appearance of the blood in this disease and that in chronic lymphatic leukemia (Fig. 45) is immediately apparent. The number of leucocytes seems much greater than in the most severe leucocytosis. The neutrophiles, identified by their polymorphonuclear character, are in excess of other forms. Normal lymphocytes are not present in this field. Eosinophiles and basophiles are increased in number. The presence of leucocytes which do not occur in normal blood is the striking feature in the picture, although a low power is used. These are eosinophilic myelocytes and large cells with round nuclei and considerable protoplasm which demand a higher power for close study. The red corpuscles are pale; a normoblast is seen above and another below toward the left. Blood platelets are increased in number.

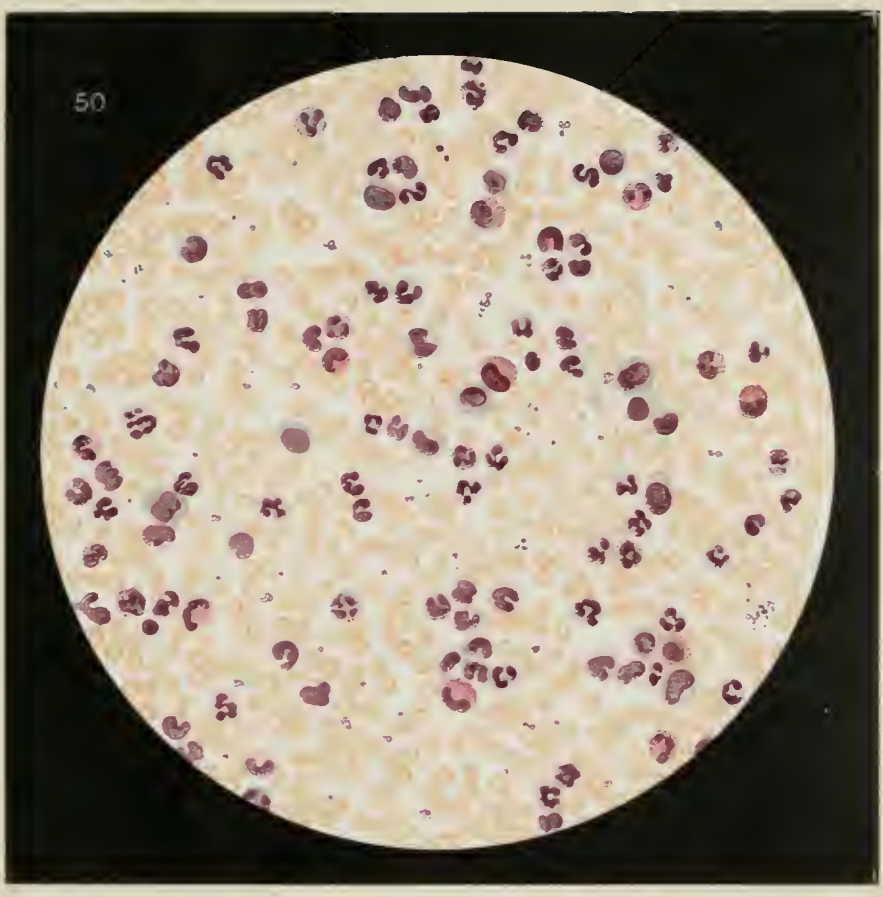

50

PLATE XXX

Figure 51.—Myelogenous Leukemia

The same specimen.

Figure 51.—Myelogenous Leukemia. Stained Film. Magnification 750

The diversity of the cellular forms in the specimen was such that all could not be included in this composite picture.

a. Polymorphonuclear neutrophile. *b*. Eosinophile. *c*. Basophile, including abnormal forms usually abundant in myelogenous leukemia. *d*. Eosinophilic myelocytes. These cells vary considerably in size, have large, pale round or indented nuclei, which are frequently indistinct. The protoplasm is basophilic and usually distended with eosinophilic granules. Some basophilic granules may be found mixed with the eosinophilic in the unusually small cells of this type. *e*. Homogeneous mononuclears with basophilic protoplasm and nuclei in different stages of development showing nucleoli. *f*. Homogeneous mononuclears with basophilic protoplasm showing slight neutrophilic granulation. *g*. A more mature lymphocyte. *h*. Disintegrating eosinophile. *i*. Nuclear remnant with nucleolus and nuclein strands. *k*. "Fragile Form."

A normoblast is present (1). Polychromatophilia and basophilic granulation in red cells can be seen. There are also many blood platelets.

No neutrophilic myelocytes present.

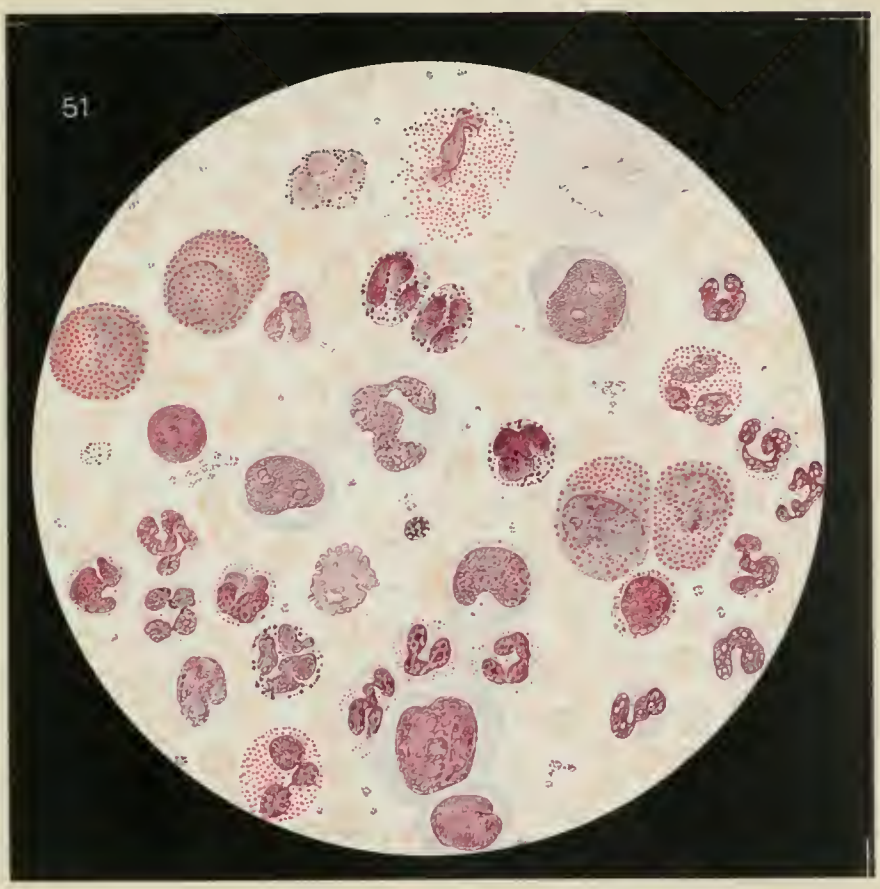

51

PLATE XXXI

Figure 52.—Myelogenous Leukemia

Myelogenous Leukemia

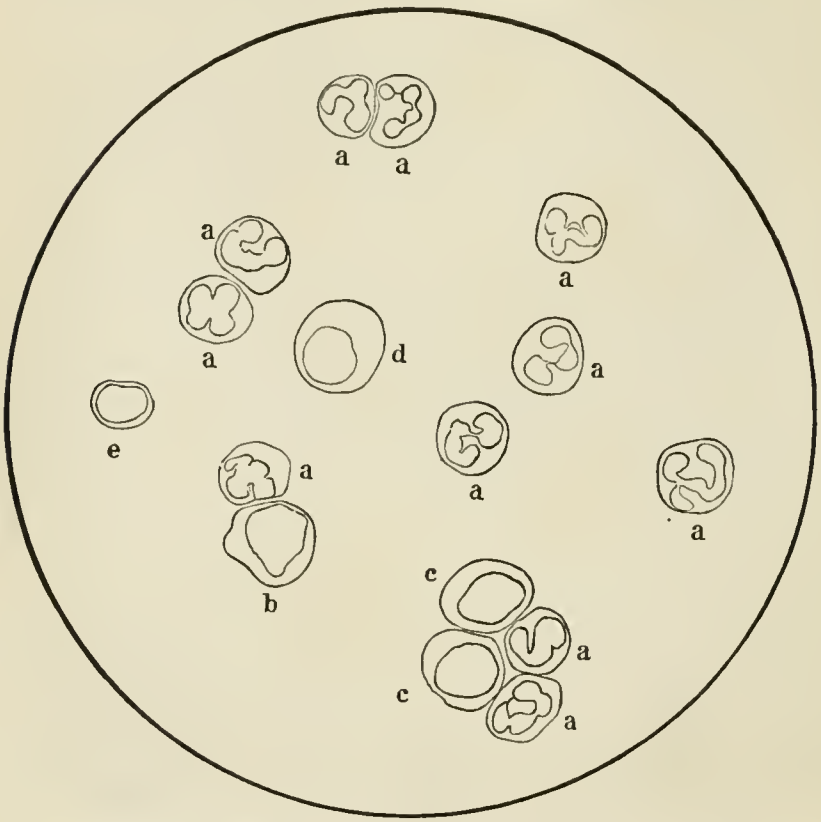
The same case after the administration of arsenic and use of X-ray. Complicated by extensive tuberculous lesion of both lungs. Two days before death.

Hemoglobin, 55 per cent.; red cells, 2,344,000; leucocytes, 78,900 in 1 c.mm. Differential count: Polymorphonuclear neutrophiles, 55,630, or 70.42 per cent.; lymphocytes, 9,270, or 11.72 per cent.; transitionals, 2,780, or 3.52 per cent.: basophiles, 930, or 1.20 per cent.; myelocytes, 10,390, or 13.14 per cent. Of the latter, neutrophilic myelocytes, 6,490, or 8.20 per cent.; eosinophilic myelocytes, 190, or 0.24 per cent.; immature stages of neutrophilic myelocytes, 3,710, or 4.70 per cent.

Figure 52.—Myelogenous Leukemia. Stained Film. Magnification 750

The character of the specimen has undergone a complete change. While a decided polymorphonuclear neutrophile leucocytosis is present, a distinct

leukemic composition is still apparent. The diminution in the number of eosinophiles, myelocytes and basophilic cells as compared with the former specimen is noteworthy; these having been replaced by neutrophilic myelocytes and immature forms of this type. This change is doubtless the result of the tuberculous infection, as it was not noted during the improvement caused by the administration of arsenic and the use of the X-ray.



a. Polymorphonuclear neutrophiles some showing vacuoles of degeneration (compare Fig. 15). *b*. Neutrophilic myelocyte. *c*. Large mononuclears with basophilic protoplasm and numerous neutrophilic granules. *d*. Large homogeneous mononuclears with neutrophilic protoplasm showing vacuoles. *e*. More mature lymphocyte.

The number of blood platelets has diminished.

Plate XXXI. Fig. 52

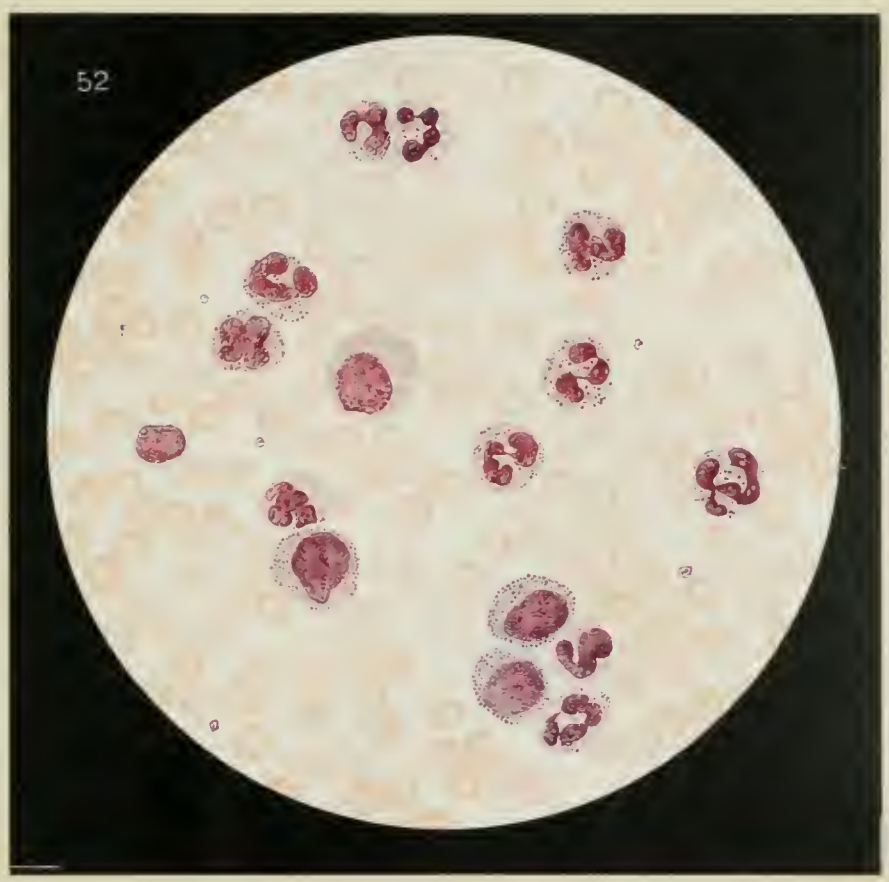


PLATE XXXII

Figure 53.—Myelogenous Leukemia

Myelogenous Leukemia

Female, 23 years old. Has looked pale for past three and one-half years. Increasing enlargement of spleen for last eighteen months. At present there is decided pallor. Spleen extends 11 cm. to the right of median line. No glandular swellings.

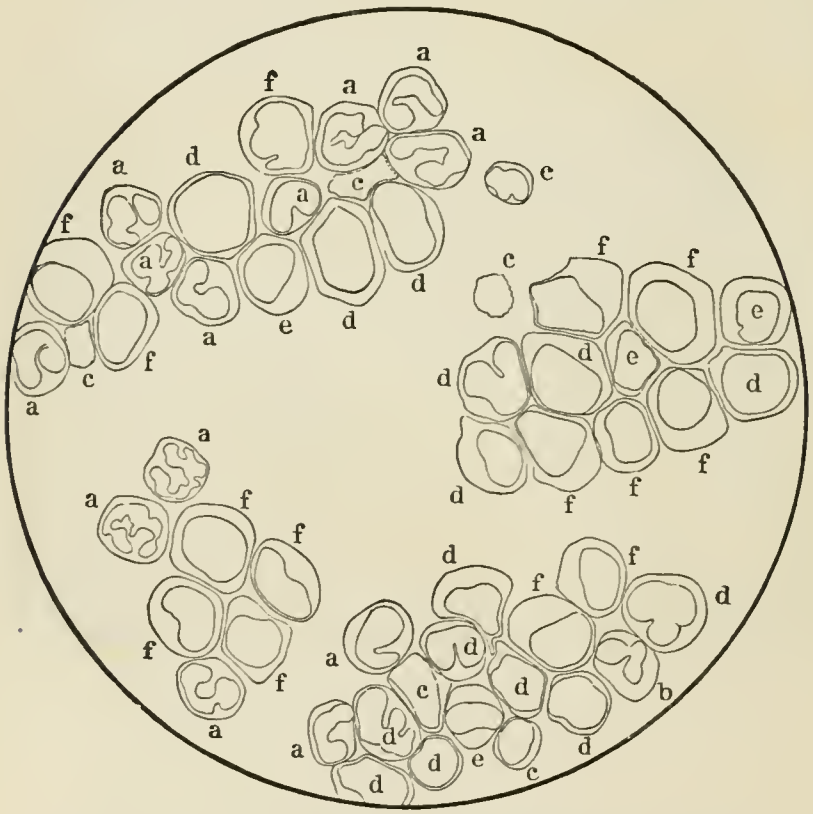
Hemoglobin, 65 per cent.; red cells, 3,200,000; leucocytes, 337,000 in 1 c.mm. Differential count: Polymorphonuclear neutrophiles, 94,040, or 27.9 per cent.; myelocytes, 195,930, or 58.10 per cent.; basophiles, 39,190, or 11.7 per cent.; eosinophiles, 7,840, or 2.3 per cent.

Diagnosis: Myelogenous Leukemia.

Figure 53.—Myelogenous Leukemia. Stained Film. Magnification 750

The complex composition of the blood seen in Fig. 51 was never noted during the entire course of this case. In this specimen the leukemic change is shown by immature forms of myelocytes, instead of by typical eosinophilic and neutrophilic myelocytes. Formerly the case would have been called a myelogenous leukemia with lymphoid condition of the blood. The white corpuscles are noted in groups of twenty or thirty and have been distorted by pressure.

The red cells show no particular change.



a. Polymorphonuclear neutrophiles. *b*. Eosinophiles. *c*. Basophilic myelocytes and basophiles. *d*. Mononuclears with more or less basophilic protoplasm. *e*. Homogeneous mononuclears with neutrophilic protoplasm. *f*. Mononuclears with basophilic protoplasm and faint neutrophilic granulation.

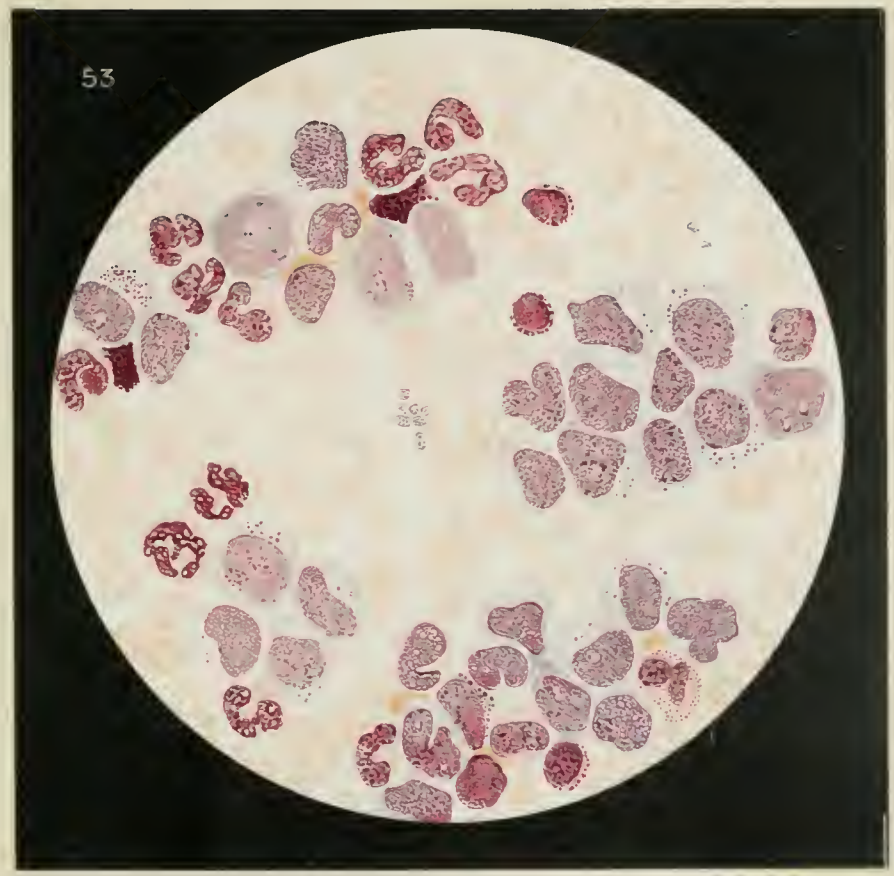

53

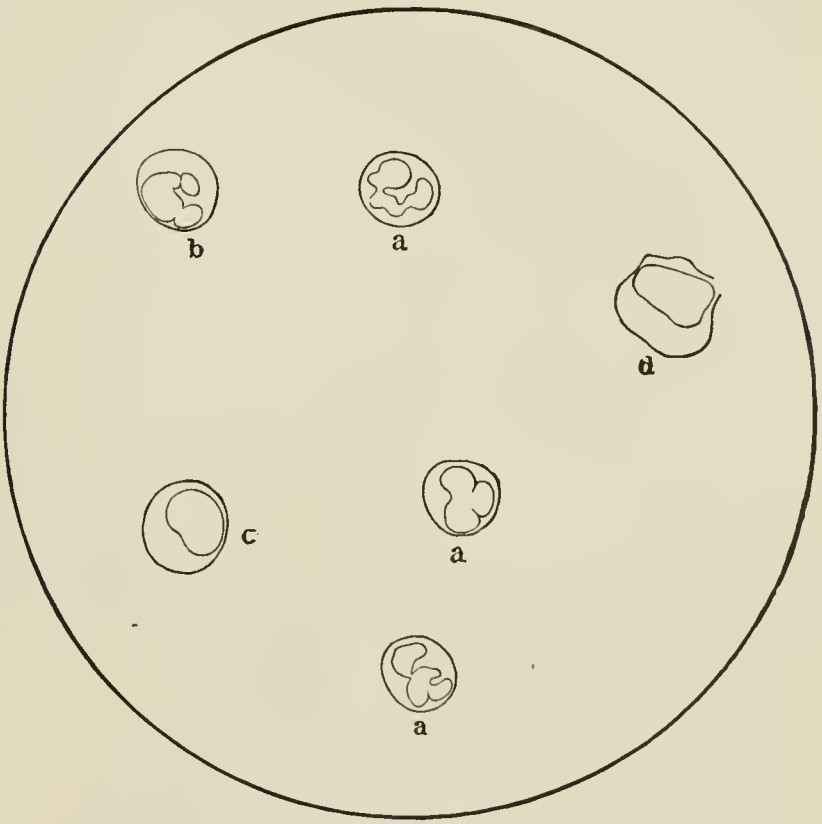
PLATE XXXIII

Figure 54.—Myelogenous Leukemia

Myelogenous Leukemia

The same case after treatment with arsenic and X-ray.

Hemoglobin, 90 per cent.; red cells, 4,050,000; leucocytes, 14,000 in 1 c.mm. Differential count: Polymorphonuclear neutrophiles, 9,520, or 68 per cent.; myelocytes, 1,820, or 13 per cent.; basophiles, 1,260, or 9 per cent.; eosinophiles, 420 or 3 per cent.; lymphocytes, 980, or 7 per cent.



a. Polymorphonuclear neutrophiles. *b*. Basophiles. *c*. Homogeneous mononuclears with basophilic protoplasm. *d*. Mononuclears with basophilic protoplasm showing neutrophilic granulation.

Figure 54.—Myelogenous Leukemia. Stained Film. Magnification 750

The condition of the blood shows decided improvement, and considerable search is necessary before two bone marrow cells are found in the same field, as in the illustration. Owing to the persistent high percentage of myelocytes the present condition must be considered a remission rather than a cure. The bone marrow cells present show no new types.

The red corpuscles show moderately diminished hemoglobin content. Some of the blood platelets are very large.

Plate XXXIII. Fig. 54

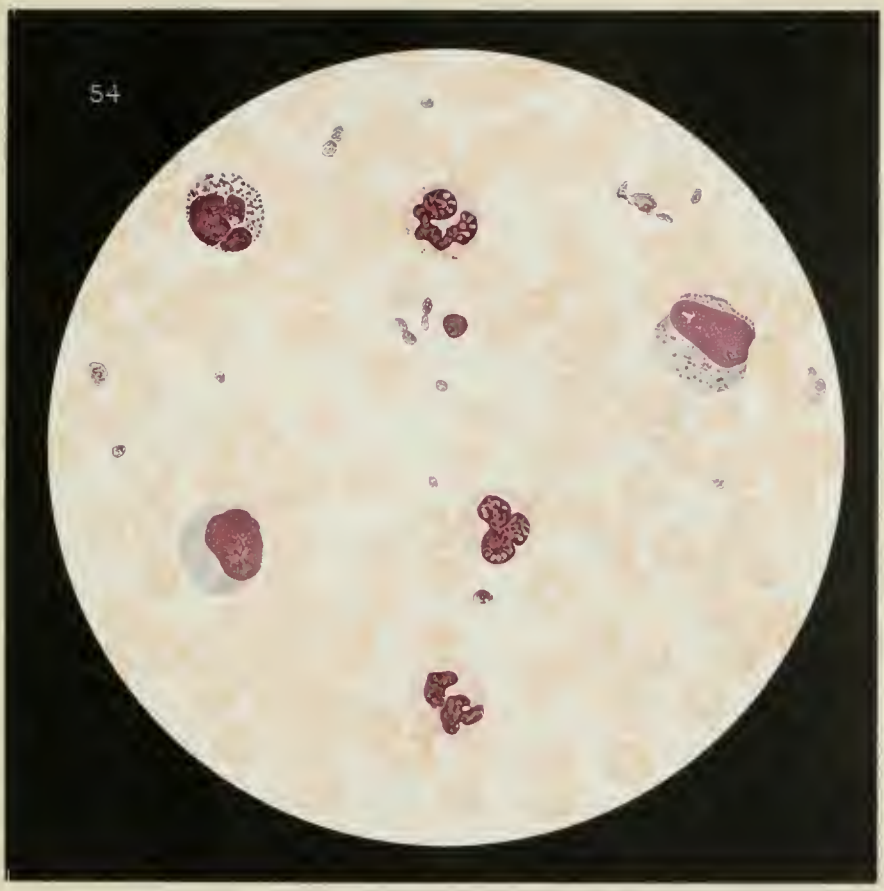


PLATE XXXIV

Figure 55.—Myelogenous Leukemia

Myelogenous Leukemia

Male, 62 years old. Suffering for the past six months from general weakness and emaciation, with enlargement of the abdomen. Moderately anemic and cachectic. No glandular swellings. The spleen extends to the median line. Blood appears concentrated. Hemoglobin, 105 per cent.; red cells, 5,000,000; leucocytes, 55,200 in 1 c.mm. Blood platelets much increased. Differential count: Polymorphonuclear neutrophiles, 38,580, or 69.88 per cent.; lymphocytes, 7,700, or 13.98 per cent.; transitionals, 390, or 0.71 per cent.; eosinophiles, 580, or 1.05 per cent.; basophiles, 580, or 1.05 per cent.; myelocytes, 7,350, or 13.33 per cent.

Numerous normoblasts, poikilocytes, polychromatophilia and basophilic granulation of red cells.

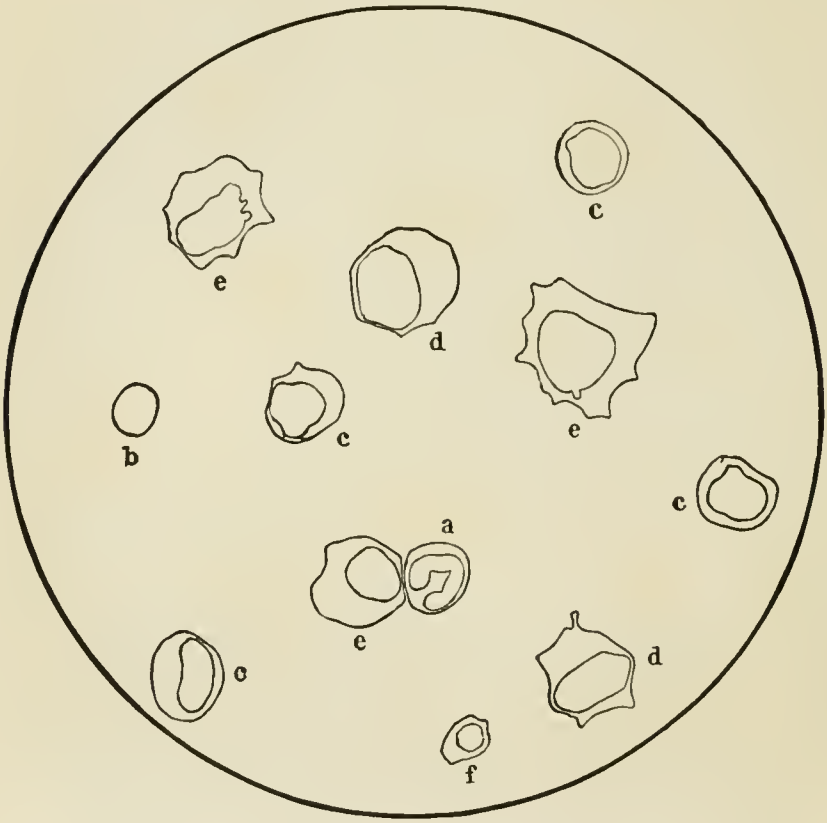
Diagnosis: Myelogenous Leukemia.

Figure 55.—Myelogenous Leukemia. Stained Film. Magnification 750

During the course of the disease this case constantly presented a condition of the blood known as "mixed cell leukemia." There is no valid reason for retaining the term in this case, or in the one described in connection with Fig. 53. In addition to neutrophilic myelocytes, there are cells representing earlier stages of development of this type, namely, mononuclears with basophilic, homogeneous or granular protoplasm.

This illustration and Fig. 53 show that all the forms of bone marrow cells need not necessarily be present in every case of myelogenous leukemia. Many specimens were examined, and not a single eosinophilic myelocyte found. As these cells develop from the basophilic myelocytes, it was not surprising to find comparatively few basophilic myelocytes and basophiles.

Subsequent developments in this case could not be followed, as the patient returned to his home.



a. Polymorphonuclear neutrophile. *b*. Immature lymphocyte. *c*. Neutrophilic myelocytes. *d*. Mononuclears with more or less marked granular protoplasm. *e*. Large mononuclears with homogeneous basophilic protoplasm. *f*. Normoblast.

Red cells show no essential change. Blood platelets are increased.

Plate XXXIV. Fig. 55

PLATE XXXV

Figure 56.—Myelogenous Leukemia

Myelogenous Leukemia

Female, 53 years old. Confined to bed for past six months. Extreme pallor and prostration. Spleen extends to right inguinal fold.

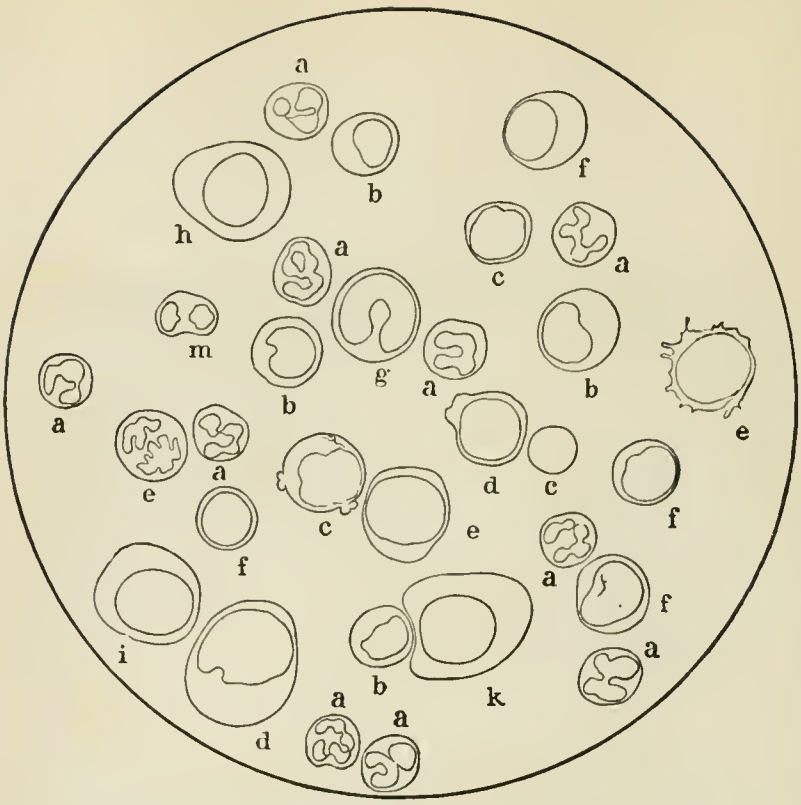
Hemoglobin, 35 per cent.; red cells, 1,843,000; leucocytes, 158,000, of which 108,000, or 68.3 per cent. are myelocytes.

Many nucleated red cells, basophilic granulation, polychromatophilia and poikilocytosis.

Diagnosis: Myelogenous Leukemia.

Figure 56.—Myelogenous Leukemia. Stained Film. Magnification 750

While the manifold cellular types in this picture resemble those in Fig. 51, closer study will show that they are quite dissimilar. The noteworthy feature is the presence of numerous bone marrow cells in various stages of development. The relative number of these cells is also greater than in the other cases illustrated, and probably due to the severity of the case and the absence of complicating lesions.



a. Polymorphonuclear neutrophiles. *b*. Eosinophilic myelocytes with nuclei poor in chromatin on which granules are also seen. *c*. Basophilic myelocytes varying in size with indented nuclei and some with densely granular protoplasm. *d*. Mononuclears with basophilic protoplasm and basophilic rather than neutrophilic granulations. *e*. Large mononuclears with basophilic homogeneous cell body. *f*. Smaller cells presumably leading to the development of lymphocytes. *g*. Early stages of transitionals. *h*. Large mononuclears with neutrophilic and slightly granular protoplasm. *i*. Undeveloped cell with more advanced development of the protoplasm than the following. *k*. Parent cell. A large mononuclear with pale homogeneous protoplasm. *l*. Megaloblast, showing mitosis, the protoplasm with basophilic granulation. *m*. Normoblast in the same condition.

Comparing this picture with Plate I will show the relative stage of development of the different cells.

The red cells show evidences of considerable anemia.

Plate XXXV. Fig. 56

PLATES XXXVI, XXXVII

Figures 57 and 58.—Acute Leukemia

Acute Leukemia

The clinical picture of these cases is characterized by high temperature and a hemorrhagic diathesis, frequently combined with ulcerative conditions in the mouth and throat, and local glandular swelling. The spleen is only moderately enlarged. The onset is acute and the general impression is that of an exceedingly severe infectious disease. A profound anemia develops rapidly and the cases invariably terminate fatally in a few days, or at most several weeks. An examination of the blood is necessary for positive diagnosis.

Recent observations indicate that a condition of the blood characteristic of chronic lymphatic leukemia or of myelogenous leukemia may also be found in acute leukemia. While the changes in the blood may vary in the different cases, usually in acute leukemia an enormous number of immature bone marrow cells are found, the normal metamorphosis into more mature forms being absent. The modern view is justified that the severely acute character of the disease with leukemic changes in the blood of one or other type is pathognomonic of acute leukemia, the disease not necessarily demanding a specific blood picture. The cause of this rapidly fatal disease is unknown, but it would seem that the extensive ulcerations in the naso-pharynx usually present, may have etiological significance.

PLATE XXXVI

Figure 57.—Acute Leukemia

Acute Leukemia

Boy, 11 years old. Acute onset with chills and uncontrollable epistaxis. Course of the disease characterized by high temperature, hemorrhagic diathesis, profound anemia, glandular swellings in the neck and secondary sepsis due to ulcerations in the naso-pharynx. Death at the end of three weeks.

Blood decidedly hydremic. Hemoglobin, 25 to 22 per cent.; red cells, 1,068,000 to 736,000 in 1 c.mm.; leucocytes, 28,300 to 11,600 in 1 c.mm. Differential count: Polymorphonuclear neutrophiles, 3.2 per cent., or 900; abnormal leucocytes, 96.8 per cent., or 27,400. No other varieties of leucocytes present. As the result of the secondary septic condition the total leucocyte count fell to 11,600, the polynuclear neutrophiles increased to 8.5 per cent., or 2,180, and the abnormal leucocytes decreased to 91.7 per cent., or 10,600. This effect of a septic complication in leukemia has frequently been noted.

Diagnosis: Acute Leukemia. Sepsis.

Figure 57.—Acute Leukemia. Stained Film. Magnification 750

The red corpuscles show all the usual evidences of a pernicious anemia, as follows: Decided pallor, microcytes, macrocytes, megaloblasts, poikilocytosis, polychromatophilia, and basophilic granulation. The decided diminution in the number of red cells is also apparent in the picture.

The abnormal leucocytes apparently belong to one cell type, but show different stages of development. Neutrophilic and occasionally eosinophilic myelocytes are also found. The abnormal cells mentioned all show more or less lobulated nuclei poor in chromatin. They have a slightly basophilic and rarely neutrophilic protoplasm, and many show a variously dense fine neutrophilic granulation. Vacuoles are sometimes observed.

These cells are identified as immature bone marrow cells, but as they are granular, they have attained a definite stage of development (see Plate I). The nuclei are decidedly indented or lobulated, and amitotic division figures in cells with a larger amount of protoplasm are frequently observed.

A certain morphological change is always observed in these leucocytes, the significance of which is still obscure. A large number of the cells show protoplasmic processes of different kinds. In some a wreath of short threads surrounds the cell, while others show one or more club-shaped projections. It would seem that these are particles of protoplasm amputated from the cell by constrictions, and partially destroyed by fixation of the specimen (see Fig. 58).

a. Polymorphonuclear neutrophile. *b*. Lymphocyte. *c*. Immature bone marrow cells. *d*. Neutrophilic myelocyte. *e*. Megaloblast.

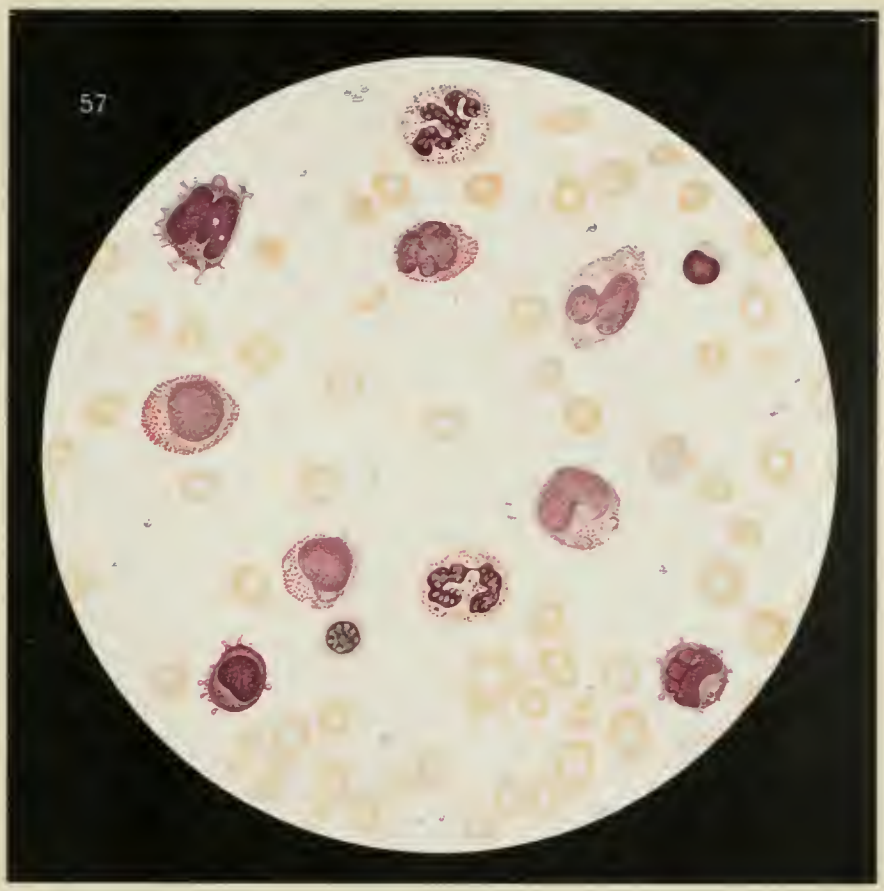

57

PLATE XXXVII

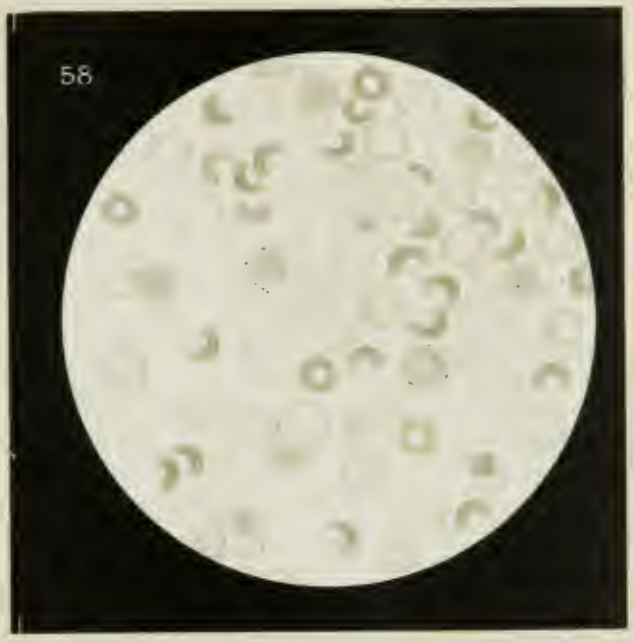
Figure 58.—Acute Leukemia

The same case.

Figure 58.—Acute Leukemia. Fresh Double Cover-glass Specimen. Magnification 750

Gentian violet has been added to the diluting fluid.

Immediately after the preparation of the specimen, a considerable number of all the leucocytes show certain globular processes as seen in the illustration. Several cyst-like structures appear attached to the cell, some being twice or three times as large as the actual cell body, the protoplasm of which is much diminished in proportion to the nucleus. The granulations are never found in the processes, but remain in what is left of the cell body.


58

BLOOD CHANGES

ASSOCIATED WITH

TUMORS OF THE BONE MARROW

PLATES XXXVIII-XL FIGURES 59-61

PLATES XXXVIII-XL

Figures 59-61.—Blood Changes Associated with Tumors of the Bone Marrow

At different stages of development certain tumors give rise to metastases in the bone marrow, with resulting changes in the morphological composition of the blood.

In circumscribed metastases, there is only an irritation of the adjacent bone marrow, the degree of which depends on the extent of the involvement. The peripheral blood shows evidence of increased or hurried regeneration, due to the increased compensating function of the remaining healthy marrow.

In other cases, there is a diffuse distribution of the metastatic process in the bone marrow, and in consequence the latter is largely replaced by tumor tissue. Under these circumstances the peripheral blood not only contains bone-marrow cells, but also shows a number of cellular varieties which justify conclusions in regard to the character and extent of the lesion. The red cells also undergo a more or less serious change and frequently show evidences resembling those of grave pernicious anemia.

PLATE XXXVIII

Figure 59.—Carcinoma of the Bone Marrow

Carcinoma of the Bone Marrow

Male, 33 years old. Pain in the left side after over-exertion in lifting a machine. One month later neuralgic pains also noted on the right side and in lumbar region. Progressive pallor.

Clinical examination: A chain of small hard glands palpable on the right side of the neck. Rapid development of bilateral choked disk. Pleural exudate on left side. Large epitheloid cells found in pleural and lumbar fluid. Sternum painful on pressure. Progressive anemia. Died at the end of ten weeks.

Autopsy: Flat cancer of stomach a little smaller than the size of a silver dollar, apparently quiescent. Numerous metastases in the bones (skull, ribs, vertebræ and pelvis).

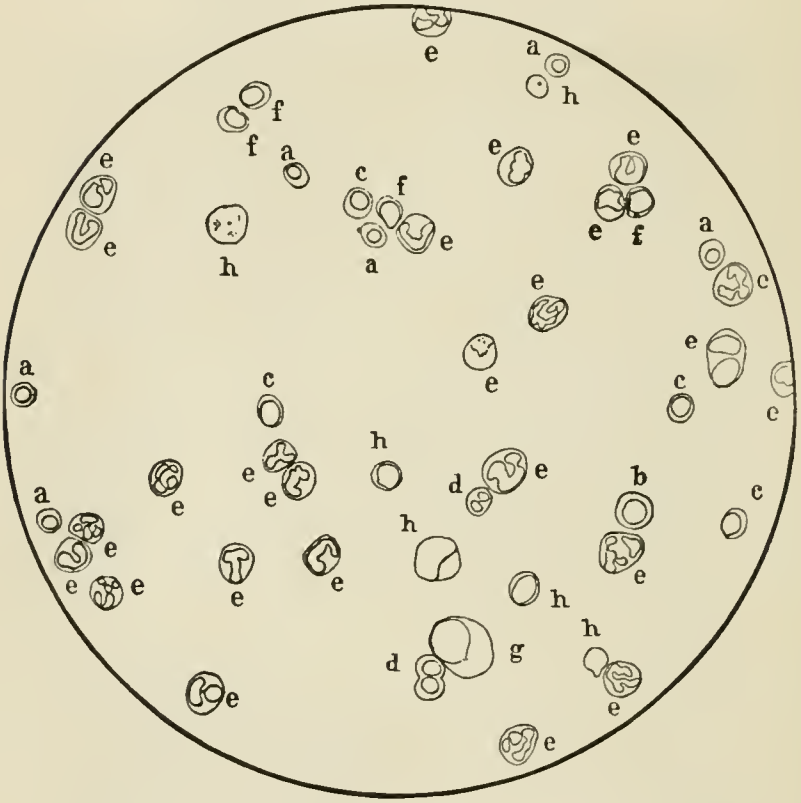
Blood examination day before death: Hemoglobin, 40 per cent.; red cells, 1,984,000; leucocytes, 16,400. Differential count: Polymorphonuclear neutrophiles, 13,440, or 82.0 per cent.; lymphocytes, 1,340, or 8.2 per cent.; transitionals, 470, or 2.9 per cent.; eosinophiles, 201, or 1.2 per cent.; myelocytes, 135, or 0.7 per cent.; "abnormal cells" (tumor cells?) 806, or 4.9 per cent. In counting 500 leucocytes, 120 nucleated red cells are seen, of which a moderate number are megaloblasts.

Figure 59.—Carcinoma of Bone Marrow. Stained Film. Magnification 330

In addition to a neutrophilic leucocytosis marked changes are present in the red cells, *i.e.*, deficient hemoglobin, polychromatophilia, poikilocytosis, and nucleated cells.

While some of these changes are referable to the secondary anemia, the presence of an unusual number of nucleated red cells is doubtless due to severe irritation of the bone marrow by the metastatic growth. The presence of numerous myelocytes in the peripheral circulation can be ascribed to the same cause, as these cells never occur in such numbers, and are frequently entirely absent in cases of secondary

or primary anemia. It is, therefore, reasonable to infer that the existing abnormal composition of the blood is referable to the active compensating function of the remaining normal bone marrow, and due to direct irritation of this medullary tissue by the metastatic lesion.



a. Normoblasts. *b*. Megaloblast. *c*. Normoblasts with polychromatophilia. *d*. Normoblasts showing amitotic division. *e*. Polymorphonuclear neutrophiles. *f*. Lymphocytes. *g*. Myelocyte. *h*. Abnormal cells (Tumor cells?).

Plate XXXVIII. Fig. 59

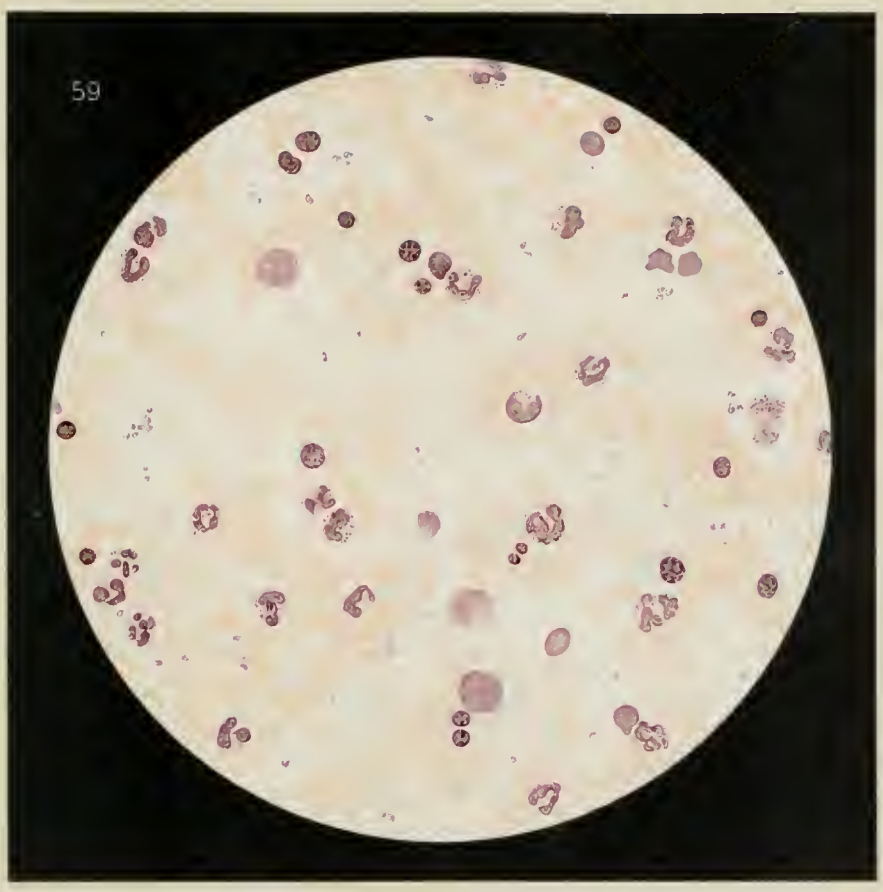


PLATE XXXIX

Figure 60.—Sarcoma of the Bone Marrow

Sarcoma of Bone Marrow

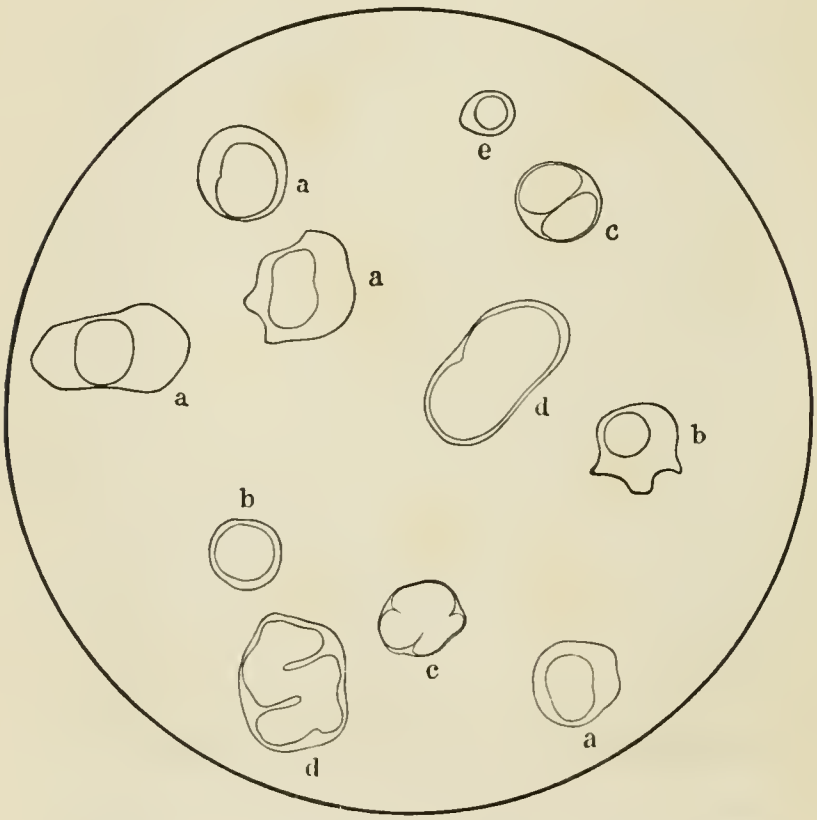
Female, 57 years old. Sarcoma of the naso-pharynx, with involvement of the local glands, and extension of the tumor to the base of the skull and the cranial cavity. In the early stages the case was supposedly a pseudo-leukemia. Secondary diffuse sarcomatosis of bone marrow. Death.

Blood examination: Fully a year before the patient's death, certain changes in the blood, such as poikilocytosis, polychromatophilia, basophilic granulation, and the presence of normoblasts justified a suspicion of the participation of the bone marrow in the disease, and led to a characteristic blood picture which persisted for several months until the patient's death. Early in the disease the condition was as follows: Hemoglobin, 60 per cent.; red cells, 3,104,000; leucocytes, 3,600 in 1 c.mm. Normal differential count. This was followed by progressive anemia, the appearance of megalocytes and many normoblasts, and cells of the lymphocyte type having larger or smaller round or indented nuclei, with more or less chromatin, and with but a narrow rim of protoplasm if any. These cells differed from the normal lymphocyte, and from the cell seen in chronic lymphatic leukemia, and closely resembled the type of which the tumor was composed. The inference seems reasonable that these were sarcoma cells which had entered the circulation.

At the height of the disease, eight weeks before the patient's death, the blood was as follows: Hemoglobin, 40 per cent.; red cells, 2,608,000; leucocytes, 7,000 in 1 c.mm. Differential count: Polymorphonuclear neutrophiles, 2,300, or 32.85 per cent.; lymphocytes, 800, or 11.42 per cent.; transitionals, 60, or 0.86 per cent.; myelocytes, 40, or 0.57 per cent.; tumor cells, 3,800, or 54.3 per cent.

Figure 60.—Sarcoma of Bone Marrow. Stained Film. Magnification 750

Composite picture. The majority of tumor cells had the appearance of (*c*) in the illustration, with large and frequently lobular nuclei, containing more or less chromatin and surrounded by a narrow rim of protoplasm. Abnormally large cells having large vesiculated or multilobular nuclei were also present as shown (*d*).



a. Myelocytes. *b*. Large lymphocytes. *c*. and *d*. Tumor cells. *e*. Megaloblast.

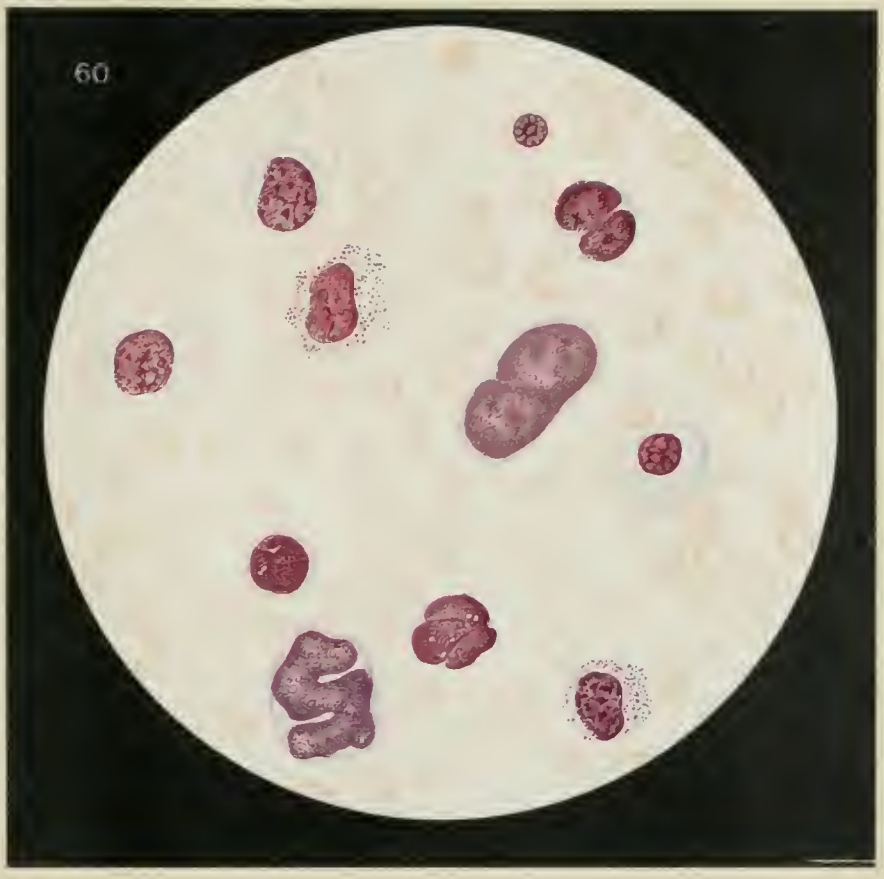

60

PLATE XI

Figure 61.—Leukosarcomatosis

Leukosarcomatosis

Sternberg recently applied this name to a clinical condition, which will demand further observation for accurate definition. The cases may closely resemble those of acute leukemia, in the sudden development of severe constitutional disturbances with high temperatures and a hemorrhagic diathesis, resulting fatally in a few days.

Concerning the gross pathology, a tumor is found in some portion of the body which has the macroscopic appearance of a lymphosarcoma (*Kundrat*), or there are changes in portions of the lymphatic system having the appearance of pseudoplasm.

The condition of the blood also closely resembles that usually found in acute leukemia, showing immense numbers of large mononuclear or multilobular abnormal cells, the average count of which exceeds 500,000 in 1 c.mm. These cells represent an atypical pathological type, which should probably not be considered as a preliminary stage of the myelocyte, but rather as a "tumor cell," it being identical with the cell found in the neoplasm present, or in the tumor-like changes of the lymphatic system.

Boy, 13 years old. Has looked poorly and anemic for a considerable time. The illness began with pain and swelling in the throat, fever and marked prostration. On admission to the hospital the patient's condition was critical. He presented numerous ulcerations of the gums, and multiple cutaneous hemorrhages about the size of a quarter, all over the body and particularly on the face, some of which were covered with scabs. The spleen was undoubtedly enlarged. Death six hours after admission.

Blood examination: Moderate anemia. Leucocytes, 560,000 in 1 c.mm.

Autopsy: The entire mucosa of the middle and lower ileum was covered with tumors the size of a hazelnut or a walnut, resembling sarcomata, and projecting into the lumen of the bowel. Hypertrophy of the lymphatic apparatus of the bowel, and of that at the base of the tongue. The bone marrow was grayish-red in color.

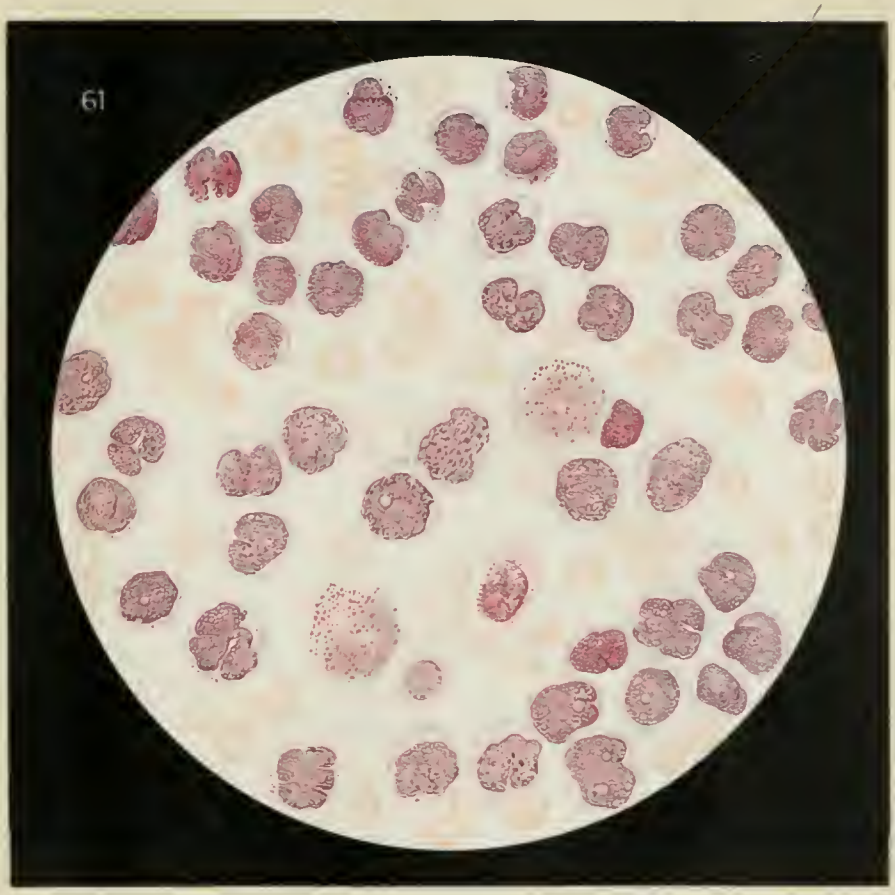
Figure 61.—Leukosarcomatosis. Stained Film. Magnification 750

A certain uniformity in the cellular types characterizes the specimen. Unsuitably or imperfectly stained films show nothing beyond many cells of similar appearance and lymphoid type. In good specimens, however, certain variations in size, configuration of nuclei and character of protoplasm can be made out in the cells. They all have round, more or less lobulated nuclei, often vesiculated in appearance, and very poor in chromatin. Several nucleoli are not uncommon. Occasionally the nucleus is indistinct and so poor in chromatin that its outline cannot be made out. The nuclei of the smaller cells show a denser structure and a greater amount of chromatin. The protoplasm is always scanty and often shows as a narrow margin, very few cells having slight neutrophilic granulation.

The conspicuous fragmentation of the nuclei is possibly a sign of pathologically rapid growth of these cells. A certain resemblance between these cells with granulation, and the leucocytes seen in acute leukemia cannot be denied. As these cells are, however, identical with those which constitute the primary tumor, they must be considered tumor cells and not bone marrow cells.

The red cells in the stained film show no essential anemic changes.

An eosinophilic myelocyte is seen below to the right, and several others were found, but with this exception no other additional or pathological blood cells could be found in the entire specimen.


61

BLOOD PARASITES

PLATES XLI-XLV FIGURES 62-71

Malarial Parasites and Trypanosomes

PLATE XLI

Figure 62.—Endogenous Development of Tertian Parasite

Figure 63.—Endogenous Development of Quartan Parasite

Figure 64.—Endogenous Development of Estivo-Autumnal Parasite

Figure 62.—Endogenous Development of Tertian Parasite. Magnification 750

Very young parasites, just after entering the red cell, present a hyaline form. In the stained specimen a distinct ring form is seen, the brilliant red chromatin appearing at one pole, with the so-called polar swelling directly opposite. These small tertian rings are not all equally distinct. Further development produces the "large tertian rings," particularly by growth of the polar swelling. Continued growth and irregular changes in form result in grotesque figures. The parasites are now approximately 24 hours old. An increase in the amount of chromatin, and the deposit of yellowish-black pigment are invariably observed at this period, and the red corpuscle, having increased to nearly or quite double its original size, is pale in color. Later the parasites appear as flattened structures, with chromatin nuclei often regularly arranged and surrounded by an achromatic zone. The chromatin nuclei increase in number, the pigment collects in a central mass or strand, and the development of the parasite is complete shortly before the febrile attack. It now presents the chromatin granules each surrounded by a

blue ring, and the whole appearing as a regular group which constitutes the sporulation form. This now bursts and the young sporozoids are free to enter other red cells to begin another 48-hour period of development.

Figure 63.—Endogenous Development of Quartan Parasite. Magnification 750

The life history is very similar to that of the tertian parasite, but 72 hours are required for the development of this form. During the first day the quartan cannot be distinguished from the tertian parasite, but later it is characterized by an absence of increase in size of the affected red cell, probably due to the smaller size of the parasite. Subsequent development usually shows a band-like structure with a large amount of pigment instead of the grotesque forms of the tertian with less pigment. The mature parasite has a smaller number of chromatin nuclei, and the sporulation form shows ten or twelve segments only, often in "sun-flower" arrangement. The small size of the quartan parasite, as compared with the tertian, is particularly apparent in the sporulation stage.

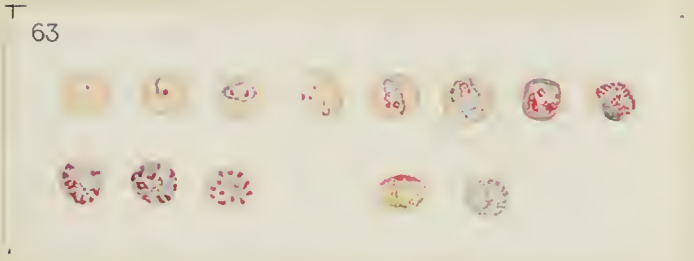
In tertian as well as quartan malaria, adult parasites are observed in the blood, which do not resemble the ordinary forms. Some have much chromatin and a weakly stained protoplasm, these being the male gametes. Others have a small amount of chromatin and a deeply stained protoplasm and are the female gametes. The sexual development of the parasites begins with these forms.

Figure 64.—Endogenous Development of Estivo-Autumnal Parasite. Magnification 750

The endogenous development of this parasite is not perfectly understood as yet. In the early ring

stage the parasites are smaller and more delicate than the tertian or quartan, but later cannot be distinguished from the latter of the same size. Crescents represent the last stage in the development of the estivo-autumnal parasite and change into oval or round bodies. The crescents are characteristic of estivo-autumnal malaria and are found during the febrile attacks as well as in the intervening quiescent periods, whereas the ring form is found in the febrile stage only. The crescents also develop in the red cells and are often seen surrounded by a halo of hemoglobin representing the remnant of the erythrocyte. In other crescents the shell of the red corpuscle is drawn like a thread between the poles of the parasite, giving rise to basket-shaped figures. Both poles of all crescents are more deeply stained than the center, which contains chromatin and pigment. The gametes, or forms for the sexual development, are derived from the crescents and have the same characteristics as those of tertian or quartan malaria.


62


63


64

PLATE XLII

Figures 65-66.—Parasites of Tertian Malaria

Parasites of Tertian Malaria

Male, 28 years old. Had malaria in Algiers while serving in the army. Develops a relapse after his return to Germany. Many tertian parasites are found in the blood.

Diagnosis: Tertian Malaria.

Figure 65.—Tertian Malaria. Fresh Double Cover-glass Specimen

The recognition of the malarial parasite is more difficult in fresh blood than in the stained film. Rings and young parasites with but little pigment may escape attention, though the mature ones should be easily seen on account of the active flowing and circulating motion of their brownish-black pigment.

A visible enlargement of the red cells containing the parasites in any stage cannot be made out. The parasite usually occupies the center of the red cell and abstracts its hemoglobin, which is converted into melanin, thus accounting for the pallor of the corpuscle. In the sporulation forms, which are rarely seen, the pigment lies in the center of the occasionally rosette-shaped parasite.

Two adult parasites and one sporulation form are seen in the illustration, and are easily differentiated from the leucocyte in the center.

Male, 20 years old. Has always been well and never away from Baden. Develops chills some time after having been severely bitten by mosquitoes. The town in which patient lived contains many Italians who arrive from home each spring.

The blood film shows a moderate number of tertian parasites.

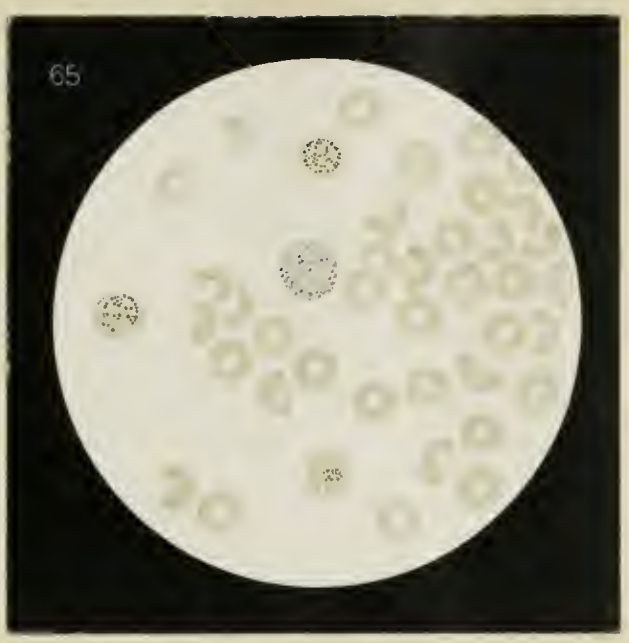
Diagnosis: Tertian malaria.

Figure 66.—Tertian Malaria. Stained Film. Magnification 750

The specimen, obtained during the chill, shows a young tertian ring and a mature sporulation form. The ring, which shows two lateral indurations instead of a polar swelling, is about to enter the red corpuscle.

The sporulation form still lies within the pale, scarcely visible erythrocyte. The somewhat regular arrangement of the youthful forms is evident, each chromatin nucleus being surrounded by a light achromatic zone believed to be nuclear juice. The pigment is seen as a slender strand.

In view of the recent and moderately severe infection, the red cells show no anemic changes.


65


66

PLATE XLIII

Figures 67-68.—Parasites of Tertian Malaria

Schoolboy, 15 years old. Develops chills on his return from Italy. Duration of illness, six days. Numerous tertian parasites in blood specimen.

Diagnosis: Tertian Malaria.

Figure 67.—Tertian Malaria. Stained Specimen. Magnification 750

The specimen was obtained a few hours before the febrile attack, and shows tertian parasites in various stages of development. After a number of attacks have occurred, the cases show so-called "sterile forms;" parasites which do not develop beyond a certain stage. If two distinct generations of parasites, maturing at different periods, are present in the blood, they give rise to the quotidian type of the disease, and present a correspondingly complex picture.

The ring forms and the mature parasites shown in the illustration contain considerable pigment and but little chromatin. The delicate red and black granulation in the red-cell host is noteworthy, and since it has been observed with the tertian parasite only, may be characteristic of this form.

Sailor, 26 years old. Has had malarial attacks for a period of eight weeks. No quinine administered. Decided anemia. Large spleen. Fever of the quotidian type. Numerous tertian parasites in the blood specimen.

Diagnosis: Tertian Malaria (Quotidian).

Figure 68.—Tertian Malaria. Stained Film. Magnification 750

The specimen contains a large number of parasites, and red cells are seen into which several ring forms have penetrated. This is believed to be indicative of the estivo-autumnal type, but the type of the fever, the presence of many mature parasites, and the slight granulation of the affected erythrocytes would indicate the tertian type.

The red cells show slight anemic changes.


67


68

PLATE XLIV

Figures 69-70.—Parasites of the Quartan and of the Estivo-Autumnal Types

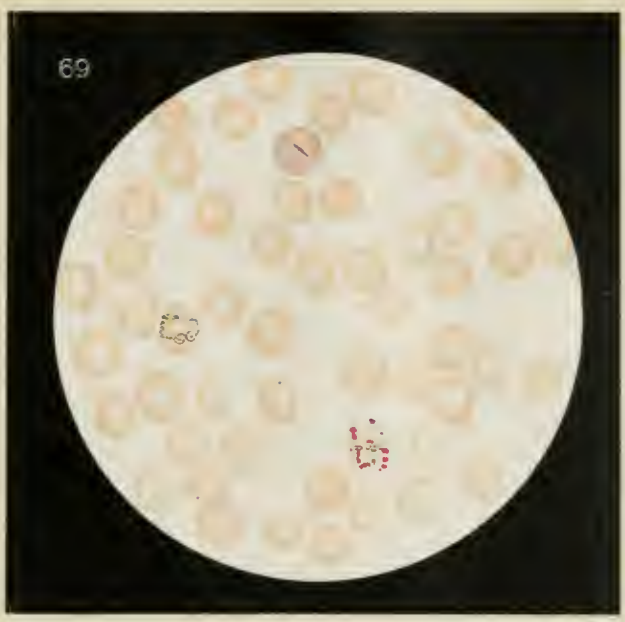
Figure 69.—Quartan Malaria. Stained Film. Magnification 750

Three malarial parasites are seen in the field. The upper one consists of a narrow band passing through the red cell. There is a fine line of chromatin granules lying beside the body of the parasite, which is stained blue. A more mature quartan is seen on the left, in the form of a broad band with considerable pigment and beginning increase of chromatin. The band form characterizes the quartan parasite, and in the more mature form shown in the lower part of the field, the small size, the slight degree of distortion, and the small number of chromatin granules are the differential points.

Figure 70.—Estivo-Autumnal Malaria. Stained Film. Magnification 750

Two delicate rings and a crescent are seen in the field. In recent infections, and after repeated relapses, both rings and crescents are invariably found in the peripheral blood. In chronic malaria crescents are frequently present in considerable numbers, but the ring form is not found. In cases of malarial cachexia it may be impossible to find parasites.

The small rings are more delicate in structure than the broader ones of tertian or quartan cases. The crescents show distinct polar stain, considerable pigment, and are surrounded by the basket-shaped outline of the red cell, exceeding in size the diameter of the erythrocyte.


69


70

PLATE XLV

Figure 71.—Human Trypanosomiasis

Trypanosomiasis

Human trypanosomiasis is due to parasites of the blood called trypanosomes, which belong to the flagellated protozoa. The parasites are actively motile in fresh blood and show the following characteristics in the stained film: They are fish-shaped and very slender, two or three times as long as the diameter of a red cell, with a long flagellum at the anterior extremity, and an undulating membrane on one side. A rather large nucleus with chromatin tint is found in the center. A bright red granule, the centrosome, is seen near the posterior blunt end, from which a fine line of red chromatin extends along the margin of the undulating membrane, into the flagellum. The body of the trypanosome takes a blue plasma stain. These parasites live in the plasma and not in the corpuscles of the blood, and multiply by longitudinal fission.

Trypanosomiasis may take an acute or chronic course, the symptoms consisting of an irregular fever, anemia, emaciation, enlargement of the spleen and glandular swellings. The parasites may exist in the blood of man for years without giving rise to clinical evidences. In most cases they pass from the blood into the cerebrospinal fluid and occasion "sleeping sickness," which is a symptom of trypanosomiasis.

The disease is communicated to man by a fly (glossina palpalis), the sting introducing the parasite into the circulation. It is possible that they develop in the glossina, or they may undergo a process of development similar to that of the malarial parasite in the anopheles.

Figure 71.—Human Trypanosomiasis. Stained Film. Magnification Approx. 1,000

The specimen, which was obtained from a European, contains but few trypanosomes. The lower parasite in the illustration shows a twisted body, the undulating membrane and chromatin thread, which becomes continuous with the flagellum, are plainly visible. The protoplasm of both parasites shows a slightly granular appearance.

Plate XLV. Fig. 71